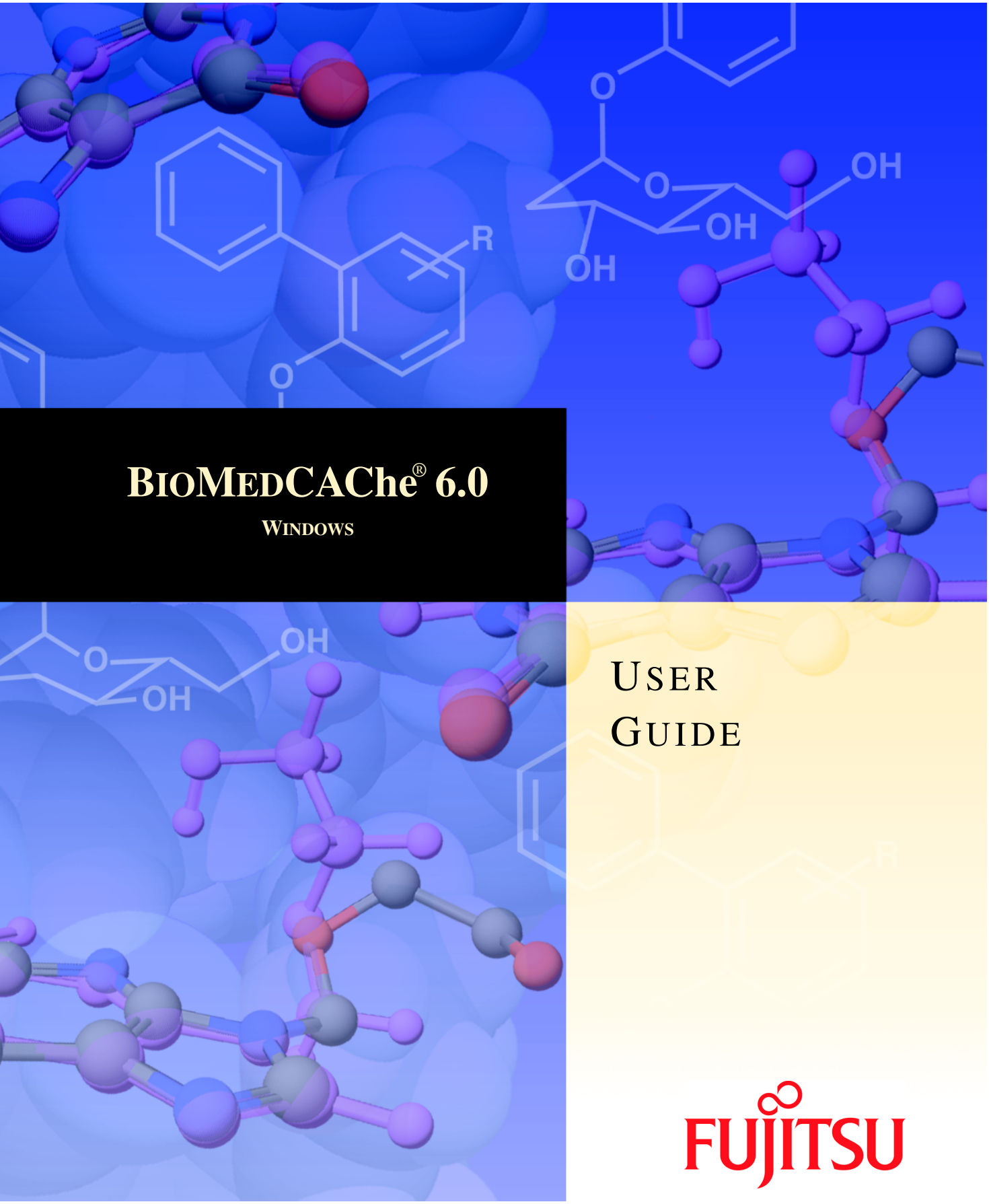


BioMedCACheⓇ 6.0

Windows

User Guide

FUJITSU

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This version of the User Guide was published in January 2003.

FJ1290-04

Contents

Support and further information iv

Introduction to the User Guide 1-1

The BioMedCAChe documentation set 1-2
New users 1-3
About this user guide 1-4
Conventions in this user guide 1-6
Navigation aids 1-8

Introduction to CAChe 2-1

Overview of CAChe 2-2
Introduction to computer-aided chemistry 2-7
The advantages of CAChe 2-8
Performing experiments with CAChe 2-12
Computational chemistry and CAChe 2-20

CAChe Basics 3-1

Starting the CAChe workspace 3-2
The CAChe interface 3-3
The application window 3-4
The workspace 3-7
Using CAChe 3-16
Using CAChe Help 3-42
Quitting CAChe 3-44

Creating Chemical Samples 4-1

Working with chemical sample files 4-2
Drawing a molecule in the workspace 4-4
Completing your molecule 4-9
Perfecting your molecule 4-10
Saving files 4-16
Printing files 4-21

Modifying Chemical Samples 5-1

Modifying atoms and bonds 5-2
Selecting workspace objects 5-3
Changing atom and bond properties 5-17

Viewing Chemical Samples 6-1

CAChe display options 6-2
Using CAChe model types 6-4
Changing the appearance of atoms 6-8

Hiding atoms 6-18
Changing the appearance of bonds 6-21
Hiding bonds 6-28
Viewing selection only 6-30
Coloring by molecules 6-31
Viewing multiple windows 6-32
Viewing chemical sample data 6-33
Changing view settings 6-37
Saving settings 6-51
Building crystal structures 6-54

Manipulating Molecules 7-1
Using the manipulation tools 7-2
Manipulating portions of your molecule 7-9
Using faster motion mode 7-12
Duplicating molecules 7-13
Deleting portions of your molecule 7-18
Fusing ring structures 7-21
Grouping atoms 7-24

Investigating Molecular Geometry 8-1
Working with chiral centers 8-2
Mirroring a molecule 8-5
Superimposing molecules 8-6
Specifying angles and distances 8-12
Working with geometry labels 8-19
Locking geometry labels 8-28
Locking atoms 8-31
Disabling locked geometry 8-34
Working with search labels 8-36

Manipulating Biomolecules 9-1
Viewing biomolecules 9-2
Working in the Sequence View window 9-10
Changing biomolecules 9-23
Comparing biomolecules 9-31

Performing Workspace Experiments 10-1
Introduction to workspace experiments 10-2
Setting up a workspace experiment 10-4
Running an experiment 10-17
Viewing active experiments 10-26
Viewing server information 10-28
Size and element limitations 10-30
Troubleshooting experiments 10-31

Viewing experimental results 10-35
Viewing log files and output files 10-39

Using the Procedure Editor 11-1
The Procedure Editor 11-2
Starting the Procedure Editor 11-3
The Procedure Editor interface 11-4
Managing the experiment environment 11-8
Showing properties of a component 11-13
Modifying a procedure 11-17
Editing the settings of a compute engine 11-23
Creating experiments 11-25
Expert modification 11-30
Creating a group procedure package 11-31
Exporting environment components 11-37
Quitting the Procedure Editor 11-38

Using ProjectLeader 12-1
Introduction to ProjectLeader 12-2
Starting ProjectLeader 12-4
Using the ProjectLeader workbook 12-6
Opening a ProjectLeader project 12-10
Adding chemical samples 12-11
Viewing sample properties 12-15
Running a ProjectLeader experiment 12-18
Using scatter plots 12-25
Changing workbook display options 12-31
Viewing cell information 12-37
Printing files 12-38
Exporting a ProjectLeader worksheet 12-41
Saving a ProjectLeader project 12-42
Quitting ProjectLeader 12-43

Optimization and Energy Calculations 13-1
Optimizing chemical samples 13-2
Selective optimization 13-5
Viewing optimized structures 13-9
Calculating current energy 13-10

Investigating Low-energy Conformations 14-1
Generating energy maps 14-2
Viewing map files 14-11

Investigating Electron Distribution 15-1
Investigating electron density surfaces 15-2

Generating an electrostatic potential surface 15-6
Investigating molecular orbital energies 15-7
Viewing a surface 15-9

Investigating Atom and Bond Properties 16-1
Calculating atomic partial charge 16-2
Calculating bond properties 16-4
Viewing atom and bond properties 16-7

Investigating Reactions 17-1
Investigating transition state structures 17-2
Investigating reaction path structures 17-4

Investigating Spectra 18-1
Investigating infrared spectra 18-2
Investigating UV-visible spectra 18-6

Investigating Biomolecules 19-1
Investigating peptide conformations 19-3
Creating a homology model of the MC4R 19-14
Docking Agouti-Related Protein into the MC4R 19-20

CAChe Computational Applications 20-1
Understanding Mechanics 20-2
Understanding Dynamics 20-7
Understanding MOPAC 20-11
Understanding Tabulator 20-22
Understanding DGauss 20-23
Understanding CONFLEX 20-34

CAChe BioComputations 21-1
Understanding Residue Names 21-2
Understanding Protein Secondary Structure Definition 21-4
Understanding Dihedral Angles for Building Peptides 21-6
Understanding Sequence Property Predictions 21-8

Keyboard and Toolbar Shortcuts A-1
Keyboard shortcuts A-2
Toolbar shortcuts A-6

CAChe File Management B-1
CAChe folders and files B-2

Index

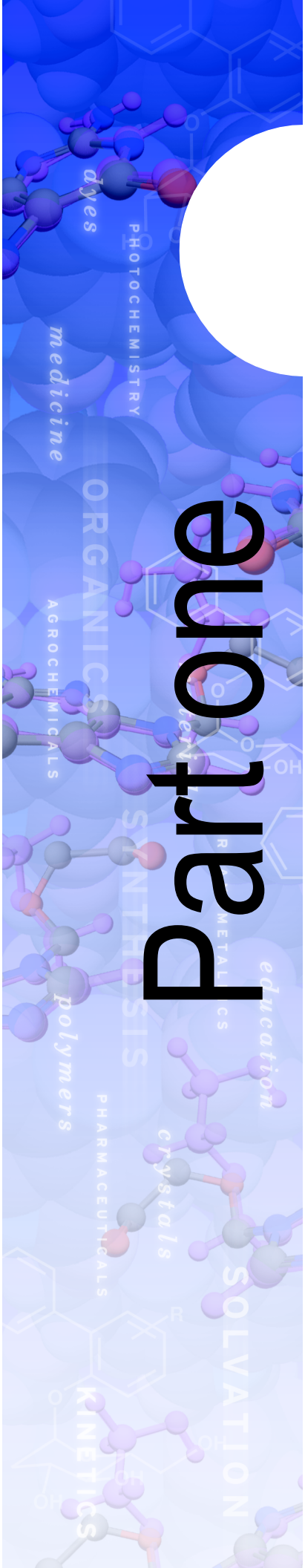
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Introduction to CAChe

The following chapters introduce you to the structure of this user guide and provide an overview of BioMedCAChe.

Chapter 1, *"Introduction to the User Guide"*, describes the conventions used in this user guide and outlines the content of each user guide part.

Chapter 2, *"Introduction to CAChe"*, introduces computer-aided chemistry and CAChe, including information about using CAChe to build, view, and analyze chemical samples; running experiments from CAChe using both the workspace and ProjectLeader; and an overview of the computational chemistry applications, including CONFLEX and MOPAC.

1 Introduction to the User Guide

Overview

This chapter describes:

- the structure of this user guide
- the text styles, icons, and navigation aids used throughout the manual.

Understanding the structure and layout of the user guide, and the conventions used throughout, will aid you in the location of specific information.

Contents

The BioMedCACHe documentation set	**1-2**	**Conventions in this user guide**	**1-6**
New users	**1-3**	**Navigation aids**	**1-8**
About this user guide	**1-4**		

The BioMedCACHe documentation set

The BioMedCACHe documentation set consists of:

- the BioMedCACHe User Guide both on-line and printed
- the BioMedCACHe Getting Started booklet both on-line and printed
- the CACHe on-line Help
- release notes for new software versions
- installation notes.

This User Guide covers the functionality of BioMedCACHe, explaining how to use BioMedCACHe, and some of the underlying concepts.

New users

If you are using BioMedCAChe for the first time, we recommend that you work through the tutorials. These can be found in the Getting Started booklet or from the CAChe menu **Help | Online Books | CAChe Getting Started**.

The tutorials are worked examples that show how to use BioMedCAChe to perform structure-guided drug discovery. In the tutorials, you learn how to clean a protein from the Protein Data Bank, analyze protein and protein-ligand interactions, display proteins as ribbons, visualize active sites, align sequences, and dock novel ligands into active sites.

For a guide to using CAChe on a task by task basis, refer to Part 3, *"Using CAChe"*.

As you use CAChe, you may find it useful to refer to Part 1, *"CAChe Basics"*, for general details on how to use CAChe.

About this user guide

This user guide describes how to use BioMedCAChe to build molecules and perform experiments on chemical samples. It explains how to use the program and gives information necessary to understand the way the program works.

The user guide is divided into parts, which are outlined below.

Introduction

This *Introduction* describes how computer-aided chemistry and CAChe can help you perform experiments on molecules. It outlines the properties that you can investigate with CAChe, and the procedures that you can apply to an experiment, as well as an overview of the experimental process.

CAChe Basics

CAChe Basics introduces the CAChe interface and describes how to use interface components such as menu options, toolbar buttons, and dialog boxes. This part also describes the tools in the CAChe workspace, which you use to build and manipulate a molecule.

Using CAChe

Using CAChe describes in detail how to use CAChe to draw and manipulate a molecule, display a molecule in different ways, measure molecular geometry, and perform experiments on a sample to investigate low-energy or transition state structures, and to discover various electronic properties.

Understanding CAChe

Understanding CAChe contains a detailed explanation of the computational applications in CAChe and the difference between these applications in their approach to experiments on chemical samples.

Appendices

The appendices list keyboard shortcuts, toolbar button functions, and the files that are added to your computer when you install your BioMedCACHe product.

Index

There is a fully comprehensive index of the BioMedCACHe User Guide at the end of the manual.

Conventions in this user guide

Before using this user guide, you should be familiar with the following:

Text styles

Different text styles are used throughout this user guide in order to emphasize the following:

Items on the interface that you need to select, such as buttons, appear as follows:

Select **Start**

Menu items are described as follows:

Choose **File** | **Open**.

i.e., Choose **File** from the menu bar, then choose the **Open** menu option from the **File** menu.

Text that you need to type in, or text that is displayed in a window, appears as follows:

```
cache@localhost
```

Icons

The following symbols appear throughout the user guide

Indicates step by step instructions for a task.

NOTE — Indicates a note.

TIP — Indicates a tip, hint, or shortcut.

Indicates a reference to another part of the user guide, or another book.



Refer to Chapter 3, *"CAChe Basics"*, for a description of the components of the CAChe interface, and an explanation of the conventions used for mouse actions such as choosing menu options, selecting tools, and using dialog boxes.

Navigation aids

There is a full table of contents for this user guide on page iii.

As explained earlier, this user guide is divided into parts, where each part contains one or more chapters.

Each chapter has a short table of contents and an overview that explains exactly what information is in the chapter.

The user guide contains many cross-references that direct you to further relevant information on a topic. However, where possible, information on any particular topic is grouped together, ensuring that you can easily locate the information that you need.

There is a comprehensive index at the end of the user guide.

2 Introduction to CAChe

Overview

This chapter introduces computer-aided chemistry and CAChe, including:

- using CAChe to build, view, and analyze chemical samples
- the accuracy of CAChe calculations compared with measured experimental data
- running experiments from CAChe using both the workspace and ProjectLeader
- an overview of the computational chemistry applications, including CONFLEX and MOPAC.

Contents

Overview of CAChe 2-10
Introduction to computer-aided chemistry 2-15
The advantages of CAChe 2-16
Calculated versus measured properties 2-17
Performing experiments with CAChe 2-20
Workspace experiments 2-21
ProjectLeader experiments 2-25
Using the Procedure Editor 2-27
Computational chemistry and CAChe 2-28
Introducing the computational applications 2-28

Overview of CAChe

BioMedCAChe is a computer-aided molecular design (CAMD) modeling tool for the Microsoft® Windows® 98, Windows® Me, Windows® XP, or Windows® 2000 operating systems. CAChe can be used to discover molecular properties and energy values. You can also draw and model molecules and perform calculations on a molecule.

BioMedCAChe and BioCAChe provide insight into biomolecule structure, properties and reactivity, including:

- similarities between potential drug molecules
- visualization of experimental structures (e.g. PDB and crystal structures)
- drug receptor interactions
- molecular shape
- design of stereo-specific candidates
- automatic sequence alignment
- location of binding sites
- design of ligands inside a binding site pocket
- partial charges
- transition states
- ribbon of proteins
- structure activity relationships (QSAR)
- superimposition of lead molecules and quality of superimposition
- bioavailability (e.g. logP)
- electrostatic interactions
- location of all low energy conformations (CONFLEX)
- Crevice maps suggest binding sites
- reactivity surfaces
- accessible surfaces
- IR spectra
- H-bond analysis
- Rule-of-5 screening

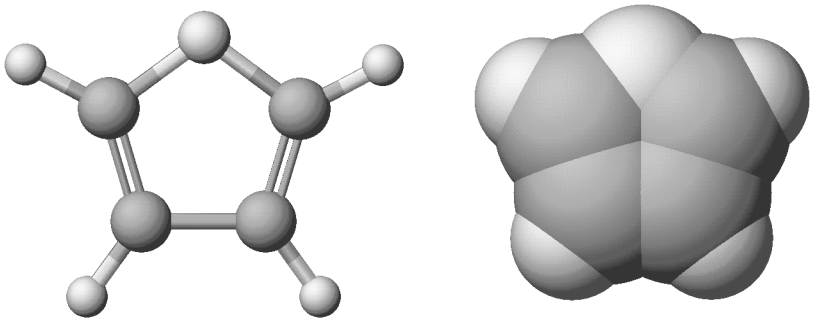
While many questions posed by biologists and medicinal chemists can be solved by using only one of these capabilities, the availability of all these working together in CAChe is invaluable.

You can draw the atoms and bonds of a molecule using the CAChe tools, copy a molecular structure from the fragment library of samples supplied with your CAChe product, or you can copy and paste a sample structure from another application, such as ChemDraw or Isis/Draw. You can manipulate this chemical sample on your computer screen, then perform experiments on it.

CAChe provides the following tools:

- drawing tools to create your molecule's atoms and bonds
- manipulation tools to rotate, scale, and move a chemical sample in three dimensions
- selection tools to modify all or part of a structure after it has been built.

You can apply a selection of modeling styles to your sample to view its structure in many different ways. The following example shows two different ways that you can view the same molecule in CAChe.



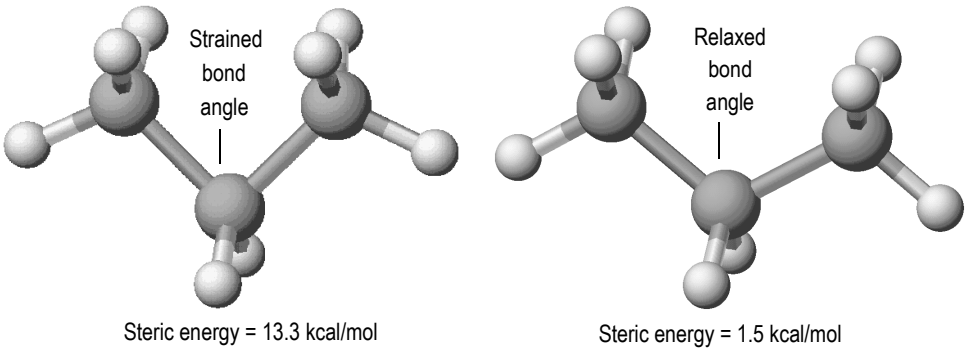
Ball & cylinder model

Space filling model

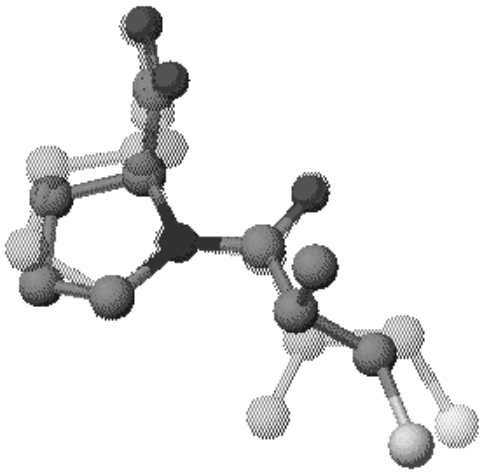
You can rotate, enlarge, and move a chemical sample around the workspace to view a molecule more closely, both before and after experimenting. CAChe shows most experimental results graphically.

CAChe can quickly and easily correct the geometry, valency, and hybridization of your chemical sample.

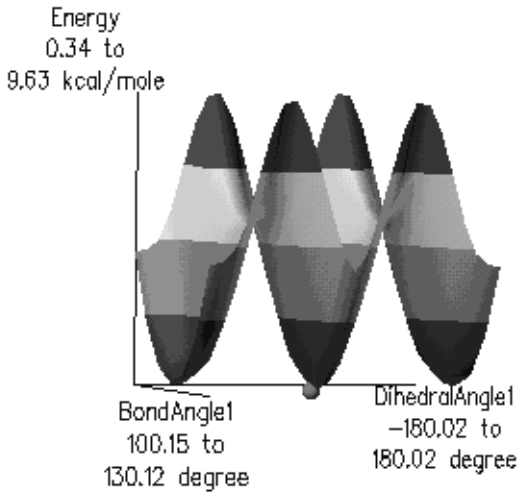
The following illustration shows a molecule before and after a CAChe optimization experiment to lower the steric energy of the molecule using calculations from classical mechanics.



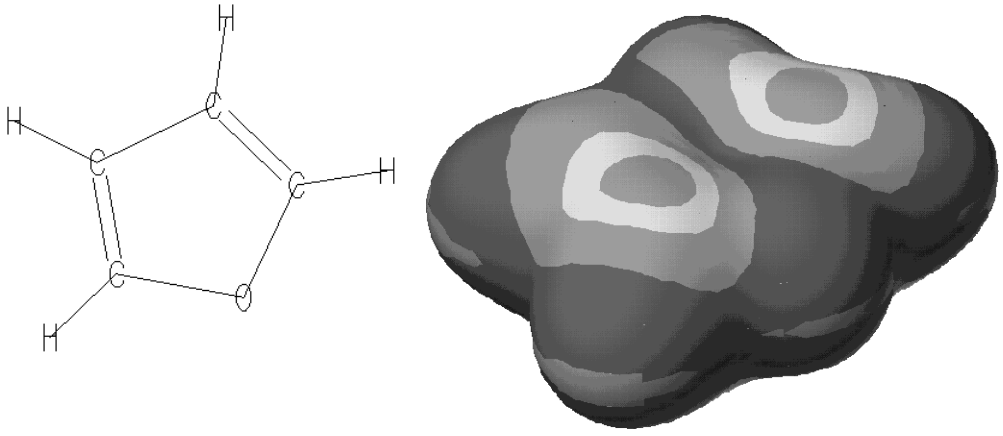
You can use CAChe to superimpose one molecule on another to highlight structural differences. The following example shows the capoten molecular structure (transparent) superimposed on the x-ray-derived capoten structure (solid).



CAChe can measure the potential energy of a series of conformations. Each conformation is either not optimized (rigid map) or optimized (optimized map). The following example shows a three-dimensional rigid energy graph.



CAChe can generate colored electron density surfaces for a chemical sample, helping you to predict certain reactive properties. The following example shows a line drawing of a furan molecule on the left. The electron density surface for the same molecule is shown on the right, colored to show susceptibility to attack by an electrophile.



CAChe ProjectLeader can help you automate calculations, track chemical samples, and maintain a history of work accomplished. The following is part of a ProjectLeader table from a quantitative structure activity relationship (QSAR) analysis of the antibiotic activity of a number of nitrofurans.This table can be used to predict the activity of additional nitrofurans. One outcome of this analysis is identification of the atoms that are responsible for activity.

ProjectLeader - [NITROFURANS (I)]

File Edit Evaluate View Format Window Help

	A	B	C	D	E	F	G	H
	Chemical Sample	experimental activity	log P	molecular formula	**Valence Connectivity Index (order 2,**	Nucleophilic Frontier Density [Atom List 1]	**QSAR 1 descr**	**Error (1)**
1	***Nitrofuran-1***	4.750	0.979	$C_8H_8N_4O_4$	2.546	0.138	4.90	0.15
2	***Nitrofuran-2***	5.050	2.905	$C_9H_8N_2O_4$	2.442	0.121	4.94	-0.12
3	***Nitrofuran-3***	5.300	0.571	$C_8H_8N_4O_4$	2.167	0.165	5.02	-0.28
4	***Nirtrofuran-4***	5.400	0.466	$C_5H_4N_2O_4$	1.759	0.170	5.43	0.03
5	***NITROFURAN-5***	5.600	2.394	$C_{11}H_8N_2O_4$	3.215	0.189	5.63	0.03
6	***Nitrofuran-6***	6.000	0.874	$C_7H_6N_2O_4$	2.169	0.163	6.09	0.09
7	***Nirtofuran-7***	7.000	0.694	$C_7H_6N_6O_3$	2.770	0.156	6.40	-0.60
8	***Nitrofuran-8***	6.000	2.012	$C_{10}H_8N_4O_3$	3.106	0.120	5.50	-0.50
9	***Nitrofuran-9***	6.600	3.938	$C_{16}H_{10}N_2O_3$	4.184	0.101	6.60	0.00
10	***NITROFURAN-10***	5.600	1.308	$C_5H_3N_1O_4$	1.551	0.197	5.82	0.22
11	***Nitrofuran-11***	5.500	1.560	$C_9H_7N_5O_3$	3.008	0.087	6.08	0.58
12	***Nitrofuran-12***	5.000	0.525	$C_8H_6N_4O_5$	3.089	0.158	5.4	0.40

Nitrofurans QSAR

- [a] B= -15.58*D + 7.97 r^2=0.73 rCV^2=0.65

Introduction to computer-aided chemistry

Computer-aided chemistry enables you to create a model of a molecular structure on a computer screen. You can move the model around the x, y, and z axes of the computer screen, and view the structure from many different angles and perspectives.

You can display the molecule as a simple line drawing, as three-dimensional spheres and cylinders, or as a combination of many different modeling styles. Use computer-aided chemistry to measure the geometry of a structure precisely and lock atom distances and bond angles at any value you require.

You can then perform experiments on the molecule, where experiments consist of calculations using classical and quantum mechanical theories. The calculations explore the characteristics of your chemical sample, predicting properties such as electron distribution, and generating conformations that possess low potential energy or heat of formation values.

Some experiments produce computer-simulated representations of the calculated properties. For example, you can view an electron density surface that predicts reactivity sites superimposed on your molecule.

Other experiments display a three-dimensional energy graph next to a series of conformations for a molecule, so you can view the relationship between energy and molecular geometry. Animate the series of conformations along an axis of the graph to compare low-energy structures that may be separated from each other by high energy barriers, or rotate the graph along any axis to view its energy values more clearly.

The experiments in computer-aided chemistry use mathematical models derived from computational chemistry to calculate molecular properties and geometries. The next section describes how CAChe applies these models during the experimental process.

The advantages of CAChe

CAChe provides you with a three-dimensional modeling tool that helps you to visualize a structure. By simply rotating and examining a model of a molecule, you can gain a new perspective and view your sample from every conceivable angle, with unmatched precision. You can zoom in on a tiny portion of your molecule, or view it from a distance. Three-dimensional ball and stick models, space-filling models, and shaded surfaces are standard CAChe modeling tools.

Chemists who use x-ray data for structure analysis want to simulate manipulating the models in space. Superimposing related samples helps compare the structural differences. Docking one sample to another can help you see steric interactions, hydrogen bond possibilities, or molecular orbital overlap.

CAChe provides all these modeling tools. Experimental results are often saved in graphical form, either superimposed on the image of the original molecule, or displayed next to the molecule as a three-dimensional graph, or series of structures that you can animate.

Geometry optimization

If you need to analyze a structure of unknown geometry, the best place to start is with an exploration of low-energy conformations of the chemical sample. Reactions usually proceed from the lowest energy conformation, or sometimes from any of several low-energy conformations with low barriers for interconversion. CAChe makes it easy to generate and analyze any number of low energy geometries.

Electronic properties

Sometimes the characteristics of a molecule can be predicted on the basis of some of its physical properties. Important properties estimated by CAChe include partial charges, bond order, electron density distribution, and molecular orbital shape.



Refer to Chapter 10, *"Performing Workspace Experiments"*, for a complete list of the properties computed by CAChe.

Graphical displays make it easier to interpret the significance of a property, and graphical comparisons are especially useful. By making it relatively easy to obtain graphical displays of a variety of electronic properties, CAChe can help you explore molecular properties and generate new ideas and draw conclusions.

Simulation of motion–dynamic models

Because molecules are not static, it may be necessary to simulate motion to understand some problems. This approach is most frequently used to model the changes in shape of macromolecules.

Modeling reaction pathways

The key to the success of modeling a reaction is locating a low energy pathway from reactants to products. CAChe models transition states to help clarify the choice between alternative pathways. By comparing computed activation energies, the selection of alternative modes of attack becomes apparent. Animation of a molecule following a predicted pathway may reveal unexpected conformational or electronic changes.

Calculated versus measured properties

Calibrating CAChe

While computer-aided chemistry is a tool that can help you in many ways, like all tools, it has some limitations.

CAChe was designed to help skilled experimental chemists explore questions that can be addressed by computational chemistry. Your chemical intuition will help you compose the right questions and CAChe will help you interpret the answers.

Even though CAChe accurately solves mathematical equations to predict chemical properties, the predicted properties do not always agree with measured properties. The disagreements arise because the mathematical model is a simplification of the real world. You can both gain confidence in the accuracy of CAChe predictions, and improve the accuracy of your predictions, by calibrating predicted results with known data.

The difference between calculated or measured values of a property and the “true” or “exact” value are referred to as ‘error’. Errors in calculated results are not the same as experimental errors; there is a fundamental difference.

Experimental errors generally fluctuate randomly about the “true” value. The average of a large number of measurements gradually approaches the “true” value.

Errors in computational methods arise because the computational method is based on a generalized model of the real world. Errors in a particular computational method are systematic, not random.

Exploiting these systematic differences makes it possible to predict properties more accurately for particular classes of chemical samples by using experimental results to calibrate the calculated predictions. The calibration holds true for other samples in the same class.

So how do you calibrate CAChe? Simply plot experimental data from similar chemical systems against calculated results and fit the plot.

Level of accuracy

Computer-aided chemistry matches a mathematical model to your chemical sample. The following table shows the level of accuracy that you can expect when you use models of molecular structures and computational chemistry. Keep in mind that even the most accurate experimental techniques are challenged to measure bond lengths with greater accuracy than 0.002Å.

	Molecular Mechanics (MM2)[a]	**Semi-empirical Quantum Mechanics (PM3)[b]**
Bond lengths	±0.005Å	0.036Å
Bond angles	±1°	±3.9°
Dihedral angles	±5°	±14.9°
Heats of formation	±0.7 kcal/mol	±7.8 kcal/mol

a. N. L. Allinger, comments made during a lecture at the QCPE Workshop on semi-empirical and *ab initio* techniques, July 1986, at the University of Oxford, England.
b. James J. P. Stewart, *J. Comp. Chem*., 1989, 10, 209–220.

Performing experiments with CAChe

The following process is a summary of how to run an experiment in CAChe :

1. Build your molecule in a chemical sample file and view it from different perspectives by moving it around the screen, rotating it in three dimensions, and scaling it.

   CAChe uses chemical sample (`.csf`) files to display and save molecules and associated data. After you have created a new chemical sample file in the workspace, the menu and workspace will display options to modify and manipulate the molecular structure. You can view your molecular structure from any angle.

2. Review what you know about your chemical sample and what you want to learn.

   A good problem-solving technique is to write down everything you know about a problem before trying to solve it. Then make a list of the properties you want to discover/uncover.

   You could ask yourself many questions about your particular project. It isn't the answers you possess at the moment that are important, but the fact that you have looked at your problem closely enough to know what answers will help you.

3. Based on your chemical sample and the properties you are interested in, run a CAChe experiment to generate the desired data.

   In choosing experimental settings, remember that in most cases, the standard settings are a good place to start.



Refer to *"Introducing the computational applications"*, p 2-20, for an overview of the computational applications.

Refer to Chapter 11, *"Using the Procedure Editor"*, for details about creating experiments and modifying procedures.

Refer to Chapter 20, *"CAChe Computational Applications"*, for more detailed information about using procedures other than the standard settings.

You can perform experiments on a chemical sample and its conformation, or on an atom or bond. You can also discover a transition state and reaction path for a chemical reaction between two samples.

4. Once you have finished running experiments, take a look at the results.

   Some experimental results can be viewed from the chemical sample file. For example, properties such as atomic partial charge or bond strain can be viewed by coloring or scaling atoms and bonds. Isosurfaces representing electronic properties can be superimposed on the molecule in the chemical sample file.

   Other experiments produce a separate file, such as a map file, where you can view and analyze experimental data in the form of three-dimensional graphics which can be manipulated in the same way as a molecule in a chemical sample file. For example, you could animate a series of low-energy conformations while viewing the corresponding value on an energy graph, or rotate the graph around the x, y, and z axes.

5. Use what you have learned to plan new experiments or create new chemical samples.



Refer to Chapter 10, *"Performing Workspace Experiments"*, Chapter 11, *"Using the Procedure Editor"*, and Chapter 12, *"Using ProjectLeader"*, for a detailed description of the experimental process in CAChe .

Workspace experiments

You can use the the CAChe workspace to build and view your molecule and its properties and investigate molecular geometry.

When you perform an experiment from the workspace, you can choose to investigate the properties of the following:

- a chemical sample
- an atom
- a bond

- a chemical sample conformation
- a chemical reaction.

Chemical sample experiments

CAChe can perform a variety of experiments on a chemical sample from the workspace, including:

- **Optimized geometry** — optimizes the geometry of your chemical sample using procedures from either classical molecular mechanics, or semi-empirical quantum mechanics. Procedures that use classical methods are the fastest and usually give good results.
- **UV-visible transitions** — generates a UV-visible spectra for a molecule, created by electron transition between molecular orbitals as electromagnetic radiation in the visible and ultraviolet (UV-visible) region is absorbed by the molecule.
- **Heat of formation** — calculates the energy of a chemical sample at a geometry-optimized energy minimum.
- **Current energy** — calculates the energy of a chemical sample at its current geometry.
- **Electron density** — generates an electron density isosurface for an electron probability density of 0.01 e-/$Å^3$. The surface is colored to reflect the electrostatic potential at every point on the surface.
- **HOMO and LUMO** — calculates the energies and shapes of the HOMO and LUMO of your chemical sample using a quantum mechanical application.
- **All molecular orbitals** — generates the shapes and energies of all of the Molecular Orbitals (MOs) in your chemical sample.
- **Susceptibility (electrophilic, nucleophilic, and radical)** — creates a three-dimensional surface superimposed over your chemical sample that indicates areas that are vulnerable to an attack by electrophiles, nucleophiles, or radicals.

Introduction



Refer to Chapter 13, *"Optimization and Energy Calculations"*, for further details about optimized geometry.

Refer to Chapter 15, *"Investigating Electron Distribution"*, for further details about the other chemical sample experiments in the preceding list.

Refer to Chapter 18, *"Investigating Spectra"*, for further details on infrared and UV-visible spectra experiments.

Atom experiment

CAChe performs the following experiment on an atom from the workspace:

- **Atomic partial charge** — calculates atomic partial charges for every atom in your chemical sample whenever you run an experiment that includes a semi-empirical quantum mechanical procedure.



Refer to Chapter 16, *"Investigating Atom and Bond Properties"*, for further details.

Bond experiments

CAChe performs the following experiments on a bond from the workspace:

- **Bond order** — determines the actual bond order of each bond in your chemical sample using semi-empirical quantum mechanical methods.
- **Bond strain** — a purely classical mechanical quantity, calculated every time a classical mechanical calculation is carried out.



Refer to Chapter 16, *"Investigating Atom and Bond Properties"*, for further details.

Chemical sample conformation experiments

CAChe performs the following experiments on a chemical sample conformation from the workspace:

- **Rigid map** — generates a potential energy map of conformations determined by geometry search labels in the sample for each structural element you want to vary, with structures for each map point not optimized.
- **Optimized map** — generates a potential energy map of conformations determined by geometry search labels in the sample for each structural element you want to vary, with structures for each map point optimized.
- **Sequence of conformations** —generates a collection of low-energy conformations by sequentially searching an unlimited number of geometry labels. The resulting map file contains local energy minima, but does not offer information about the energy barriers between them.
- **Dynamics trajectory** — generates a trajectory of a chemical sample in random thermal motion by randomly adding kinetic energy to each atom. Motion is induced that can overcome small barriers to lower energy structures.



Refer to Chapter 14, *"Investigating Low-energy Conformations"*, for further details.

Reaction and transition state experiments

CAChe performs the following experiments from the workspace on reaction and transition state structures produced by a chemical reaction:

- **Map reaction** — generates a potential energy map of conformations determined by geometry search labels in the sample for each structural element you want to vary, with structures for each map point optimized.

- **Search for saddle** — calculates a saddle point (transition state) structure from a reactant and a product molecule of a chemical reaction.
- **Refine transition state** — refines the structure and energy of a transition state structure using a minimize gradient calculation.
- **Verify transition state** — calculates a transition state structure's vibrational transitions, where a single negative vibration confirms a true transition state.
- **Find reaction paths** — produces a map file containing the structures a chemical sample in a transition state geometry will pass through on the way to the reactant or product structures.



Refer to Chapter 17, *"Investigating Reactions"*, for further details.

ProjectLeader experiments

ProjectLeader is often the best place for a scientist to start to plan experiments. You can use CAChe ProjectLeader to perform calculations on several chemical samples at one time, or carry out statistical analyses on chemical samples, including calculations based on customizable equations.

ProjectLeader is a separate application accessible from either the Windows Explorer, or the **Start** menu on the Windows taskbar.



Refer to Chapter 12, *"Using ProjectLeader"*, for further details on starting ProjectLeader, and ProjectLeader experiments and capabilities.

Use ProjectLeader to:

- perform an experiment on several chemical samples at once (you can experiment on only one chemical sample at a time using the workspace)

- perform statistical analyses on experimental results, including multiple linear regression, forward and reverse stepwise regressions, and customizable algebraic equations
- view the values of experimental calculations for several chemical sample files at the same time
- create scatter plots of the results of experiments and analyses to view trends in your data.

Viewing and analyzing columns of experimental data for several chemical samples at once enables you to establish mathematical relationships between one set of data and another, thus aiding:

- the process of calibration by comparing the results of measurements on specific instruments and the known standard results
- the calculation of quantitative structure activity relationships (QSAR) between molecular structure and pharmacological activity, and quantitative structure property relationships (QSPR) between molecular structure and properties such as boiling points, octanol-water partition coefficients, and dipole moments.

You can use ProjectLeader to perform a variety of experiments, such as:

- atom and bond count
- net positive and negative charge for a molecule
- molecular properties such as molecular formula, weight, and refractivity
- elemental analysis calculating the percent weight of each element
- zero-order, first-order, and second-order molecular connectivity indices
- dipole moment and dipole vectors x, y, and z
- dielectric, steric, and total energy of a structure
- electron affinity

- shape index order 1, 2, and 3
- octanol water partition coefficient.

Experiments can be performed on entire chemical samples, or on chemical sample components such as atoms, bonds, and molecular orbitals.

Using the Procedure Editor

The Procedure Editor allows you to create your own experiments, and change parameter settings from the default settings supplied with CAChe.

The Procedure Editor allows you to display the experiment environment in a tree view.

From this view, you can perform a wide range of functions. These functions include:

- creating new experiments
- modifying procedures by adding, deleting, or moving steps
- editing compute engine data
- editing parameter data
- creating new packages for use by groups of users.



Refer to Chapter 11, *"Using the Procedure Editor"*, for full details about using the Procedure Editor.

Computational chemistry and CAChe

CAChe uses computational chemistry as an essential part of computer-aided chemistry. By applying computational molecular models derived from mathematical equations to a chemical sample you create, you can calculate molecular properties such as the position and behavior of electrons, and nuclei in certain conditions.

The computational chemistry tools that CAChe uses are derived from classical mechanics and quantum mechanics, and are applied to your chemical sample by a number of computational applications that perform calculations based on specified parameters.

Using classical mechanics, CAChe can:

- optimize molecular geometry
- determine a series of low-energy conformations between high energy barriers
- simulate the normal motion of atoms according to time, temperature, and the calculated forces of the atoms.

Using quantum mechanics, CAChe can:

- predict electron density and distribution in a molecule
- investigate molecular orbital energies
- optimize molecular geometry
- determine transition state geometry
- calculate molecular properties such as bond order and atomic partial charge.

Introducing the computational applications

While mostly invisible to the user, CAChe uses a number of computational applications which use classical and quantum mechanical methods to perform experiments on your chemical sample.

This section gives an overview of each computational application.



Refer to Chapter 20, *"CAChe Computational Applications"*, for more detailed information.

Mechanics optimizes molecular geometry using classical molecular mechanics. Mechanics finds an optimum geometry by systematically moving all atoms in a chemical sample until the net force acting on each atom approaches zero. Mechanics generates a log data file and an output file containing experimental details, and alters the structure of the molecule in your chemical sample file to correspond to the calculated optimum geometry.

CONFLEX generates low-energy conformers of a molecule of any shape. It can be used to compute an optimum geometry and potential energy maps.

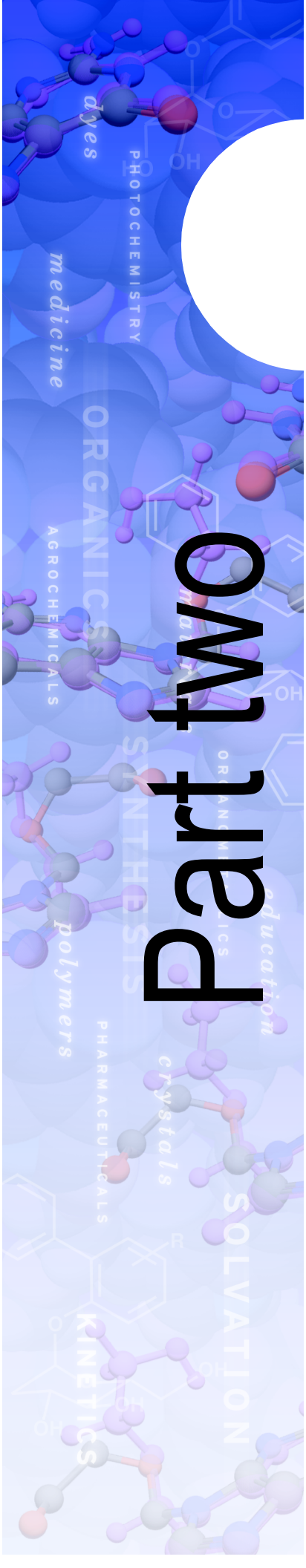
Dynamics simulates the normal motion of atoms according to time, temperature, and the calculated forces on the atoms. Dynamics generates a trajectory or collection of structures over time, where each structure has an associated potential and kinetic energy as well as temperature. A log data file and an output file containing experimental details are also generated when an experiment is performed with Dynamics. Trajectory information is stored graphically in a separate energy map file.

MOPAC is a semi-empirical quantum mechanical computational tool that provides optimization and wavefunction (electron distribution) data to search for optimized geometry, transition state geometry and molecular properties such as bond order, partial charges, and orbital energies. MOPAC includes several sets of parameters from which you can choose: MINDO/3, MNDO, MNDO-*d*, PM3 and AM1. MOPAC also implements MOZYME, a linear scaling method for giant molecules. MOPAC generates a log data file and an output file containing experimental details, and alters the structure of the molecule in your chemical sample file to correspond to the calculated optimum geometry.

Tabulator converts the solved wavefunction from MOPAC into three-dimensional graphical representations of several properties including susceptibility, electron density, molecular orbitals, and electrostatic potential. Information generated by Tabulator can be viewed superimposed on the molecule in the chemical sample file.

DGauss is a density funtional theory program. It can determine an optimum geometry and compute electronic properties such as bond order, atom partial charges and potential energy maps.

📖 NOTE DGauss is available as an optional add-on to CAChe.



CAChe Basics

The following chapter describes the basics of CAChe for Windows.

Chapter 3, *"CAChe Basics"*, introduces the components of the workspace.

3 CAChe Basics

Overview

This chapter introduces the basics of using CAChe, including how to:

- start and quit CAChe
- use the components of the workspace
- access CAChe on-line Help.

Contents

Starting the CAChe workspace **3-2**
The CAChe interface **3-3**
The application window **3-4**
The menu bar 3-4
The toolbar 3-5
The status bar 3-6
The workspace **3-8**
The title bar 3-9
The style bar 3-9
The tool palette 3-13
The scroll bars 3-14
Stereo 3D cursor 3-15
Manipulating document windows 3-16
Using CAChe **3-17**
Using the mouse 3-17
Using the menu bar 3-20
Using the toolbar 3-21
Using dialog boxes 3-22
Using the workspace selection tools 3-29
Using the Select tool 3-33
Using the workspace style bar 3-40
Using CAChe Help **3-43**
Viewing context-sensitive Help 3-43
Viewing the CAChe Help system 3-44
Quitting CAChe **3-45**

Starting the CAChe workspace

CAChe runs in a Windows Me, Windows 98, Windows NT 4.0 and Windows 2000 environment.

To start the CAChe workspace

1. Choose **Start** | **Programs** | **CAChe** | **Workspace** from the Windows taskbar.

   An initializing CAChe splash screen containing CAChe version details is displayed.

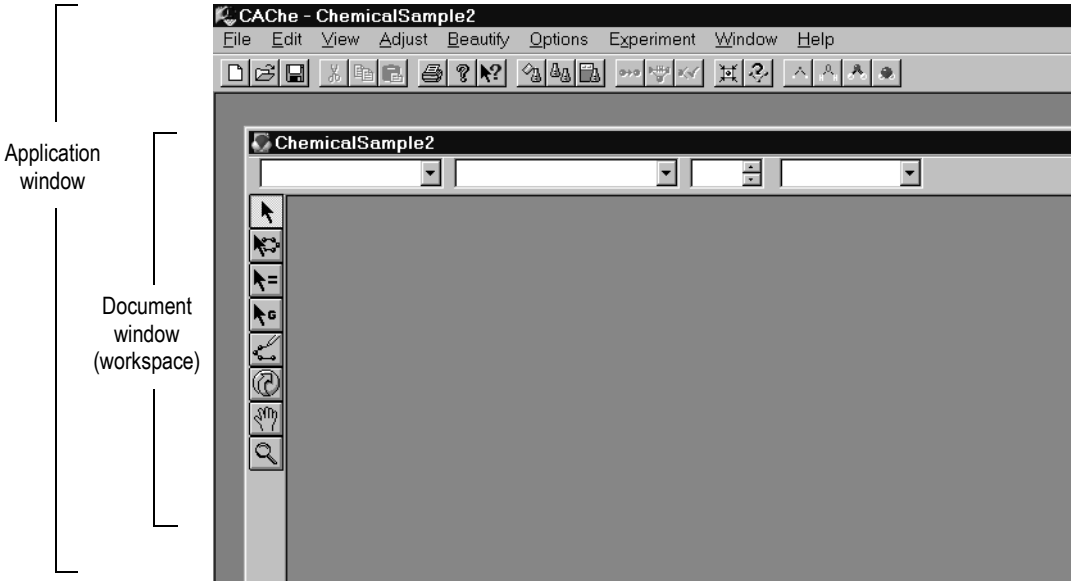
   After a few seconds, the CAChe application window opens, containing an empty document window, referred to as the workspace.

The CAChe interface

The CAChe user interface, shown below, consists of:

- an application window, containing a menu bar and toolbar
- a document window, which contains tools and drop-down lists to help you draw and manipulate your chemical sample. When the active document is a chemical sample file, the document window is referred to as the workspace. Chemical sample files are used to create, edit, and experiment on molecules.

Refer to Chapter 4, *"Creating Chemical Samples"*, for a description of chemical sample files.



The application window

The CAChe application window contains standard Windows features, such as:

- a menu bar with a selection of menu options
- a toolbar containing buttons that provide a shortcut to some of the menu options
- a status bar at the bottom of the window.

The menu bar

The menu bar displays options that give access to drop-down lists of menu options. The menu that is visible when you first start CAChe is as follows:

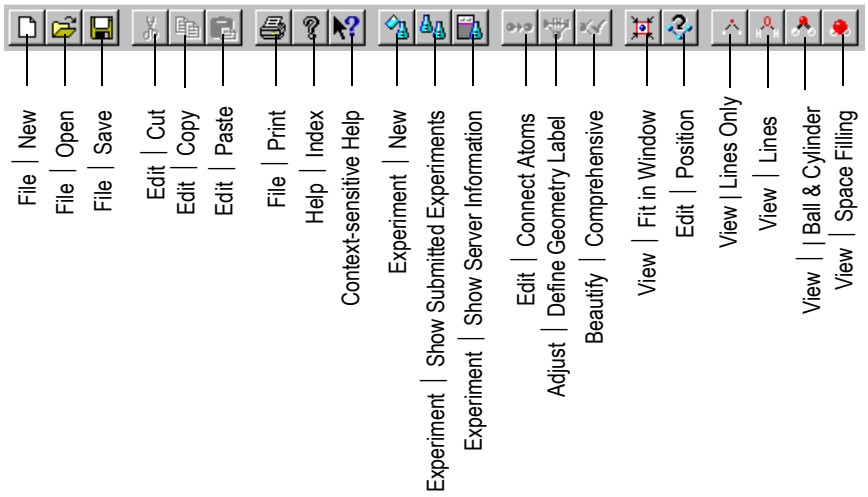


Refer to *"Using the menu bar"*, p 3-20, for details on how to use the CAChe menu.

The toolbar

The toolbar contains a collection of buttons that provide a shortcut to some of the menu options.

The following diagram shows the toolbar and the corresponding menu options that each button performs.



Refer to *"Using the toolbar"*, p 3-21, for details on how to use the CAChe toolbar, and a list of toolbar buttons and their equivalent menu options.

Hiding the toolbar

You can choose to hide the CAChe toolbar.

To hide the CAChe toolbar

1. When the toolbar is visible, choose **Options | Show Toolbar**.

   The toolbar is no longer displayed in the CAChe application window.

   The check mark next to the **Show Toolbar** drop-down list option is no longer displayed, indicating that the toolbar is currently hidden.

To redisplay the CAChe toolbar

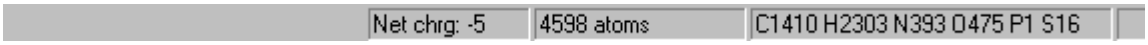
1. When the toolbar is hidden, choose **Options** | **Show Toolbar**.

   The toolbar is displayed in the CAChe application window.

   A check mark is displayed next to the **Show Toolbar** drop-down list option, indicating that the toolbar is currently visible.

The status bar

The status bar is displayed at the bottom of the CAChe application window, and describes the action performed by a selected command in a menu drop-down list, or a selected button in the toolbar. In addition, the status bar displays the net charge on the molecule, the number of atoms and the empirical formula.



When there is no drop-down list option or toolbar button selected, the status bar displays the following message:



Hiding the status bar

You can choose to hide the CAChe status bar.

To hide the CAChe status bar

1. When the status bar is visible, choose **Options** | **Show Status Line**.

   The status bar is no longer displayed.

   The check mark next to the **Show Status Line** drop-down list option is no longer displayed, indicating that the status bar is currently hidden.

To redisplay the CAChe status bar

1. When the status bar is hidden, choose **Options** | **Show Status Line**.

   The status bar is displayed at the bottom of the CAChe window.

A check mark is displayed next to the **Show Status Line** drop-down list option, indicating that the status bar is currently visible.

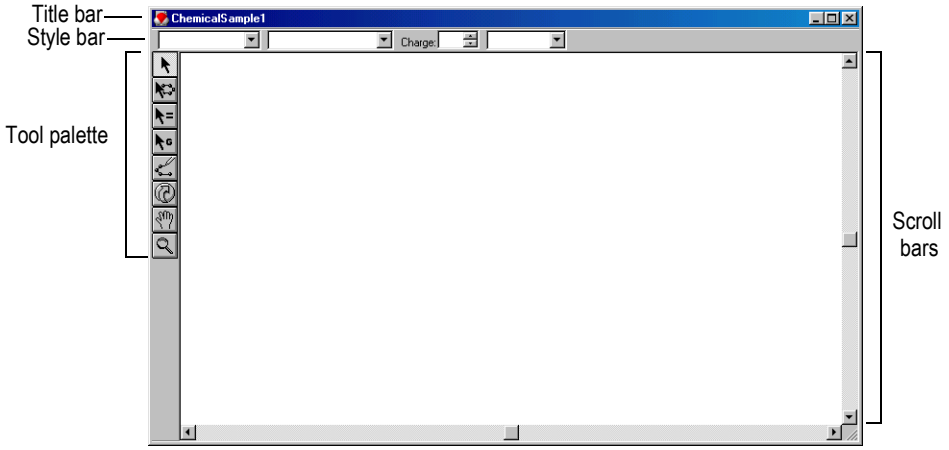
The workspace

The active document window is referred to in CAChe as the workspace. While you can have many document windows open at any one time, there can only be one active document window.

Any menu bar or toolbar commands you choose affect the active document window. To activate a window, click on it.

The main components of the workspace are:

- a title bar that displays the name of the document
- a style bar with drop-down lists that enable you to change the element type, bond type, charge, and hybridization of selected parts of your molecule
- a tool palette that provides selection tools, a drawing tool, and manipulation tools.



A blank workspace

The title bar

The workspace title bar displays the name of the document.



The workspace that appears when you start CAChe has the default name `ChemicalSample1`. To change this name, save the file. Once you save a file, a three-letter suffix appears in the document name, which describes the file type of the document.

The main document file type for CAChe is the chemical sample file, indicated by the suffix `.csf`. Use chemical sample files to:

- draw your molecule
- view your molecule in different ways
- launch experiments.

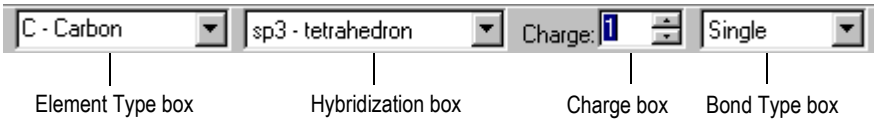
Refer to Chapter 4, *"Creating Chemical Samples"*, for more information on chemical sample files.

The workspace title bar also contains the default Windows minimize, maximize, and close buttons.

The style bar

The workspace style bar provides four items that enable you to change or create features of selected parts of your molecule, as follows:

- element type
- hybridization
- charge
- bond type.



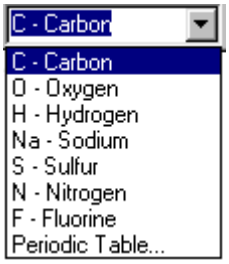
Example style bar

Use the style bar in conjunction with the workspace selection and drawing tools to:

- draw atoms of a specific element
- draw bonds of a specific bond type
- draw atoms with a specific hybridization and charge
- change the element type of selected atoms
- change the bond type of selected bonds
- change the hybridization and charge of selected atoms.

The Element Type box

The Element Type box lists the last seven elements for atoms you have drawn or selected, and provides access to the Periodic Table dialog box, from which you select any element in the Periodic Table.



Once you choose an element from the Element Type drop-down list, you can:

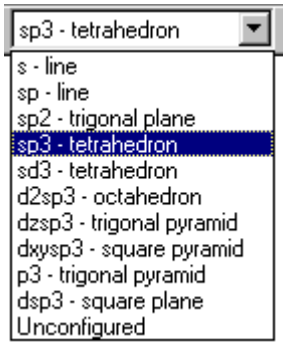
- draw an atom of that element
- change a selected atom to that element.

Refer to *"Using the workspace style bar"*, p 3-40, for information on using the Element Type drop-down list.

The Hybridization box

The Hybridization box provides a drop-down list of hybridization or electronic configuration alternatives which you can apply to:

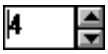
- the next atom you draw
- a selected atom.



Refer to *"Using the workspace style bar"*, p 3-40, for information on using the Hybridization drop-down list.

The Charge box

The Charge box is a text box which you can use to enter a charge value, or select a negative or positive charge value provided by CAChe, by using the up or down arrow button next to the text box.



Once you have selected or entered a charge value, you can:

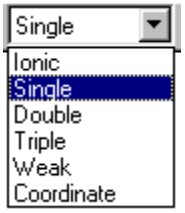
- draw an atom with the specified charge value
- change the charge of a selected atom.

Refer to*"Using the workspace style bar"*, p 3-40, for information on using the Charge text box.

The Bond Type box

The Bond Type box lists up to six bond types. Once you choose a bond type from the drop-down list, you can:

- draw a bond of the specified bond type
- change a selected bond to the specified bond type.



Refer to *"Using the workspace style bar"*, p 3-40, for information on using the Bond Type drop-down list.

Hiding the style bar

You can choose to hide the workspace style bar.

To hide the workspace style bar

1. When the style bar is visible, choose **Options** | **Show Ribbon**.

   The style bar boxes are no longer displayed at the top of the workspace.

   The check mark next to the **Show Ribbon** drop-down list option is no longer displayed, indicating that the style bar is currently hidden.

To redisplay the workspace style bar

1. When the style bar is hidden, choose **Options** | **Show Ribbon**.

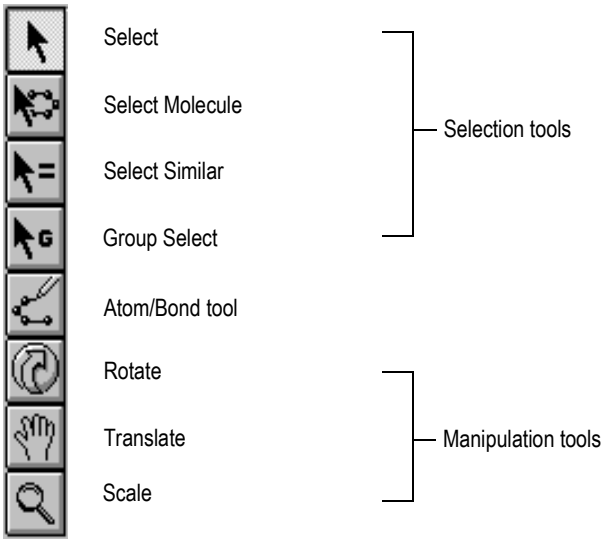
   The style bar is displayed at the top of the workspace.

   A check mark is displayed next to the **Show Ribbon** drop-down list option, indicating that the style bar is currently visible.

The tool palette

The workspace tool palette provides three types of tools:

- selection tools
- a drawing tool
- manipulation tools.



The selection tools

The tool palette contains the following selection tools:

- the Select tool, which is the default workspace tool. Use it to select individual objects
- the Select Molecule tool, which selects an entire molecule
- the Select Similar tool, which selects all objects of a similar type
- the Select Group tool, which selects an atom and all the atoms with which it shares a group.

The Atom/Bond tool

Use the Atom/Bond tool to draw atoms and bonds in the workspace. Specify element type, bond type, charge, and hybridization first by using the style bar drop-down lists.

The manipulation tools

The tool palette contains the following manipulation tools:

- the Translate tool, which moves objects in the workspace
- the Rotate tool, which rotates workspace objects in three dimensions
- the Scale tool, which zooms in and out on objects in the workspace.



Refer to *"Using the workspace selection tools"*, p 3-29, for further details about the selection tools.

Refer to Chapter 4, *"Creating Chemical Samples"*, for details about the Atom/Bond tool.

Refer to Chapter 7, *"Manipulating Molecules"*, for details about the manipulation tools.

The scroll bars

Use the scroll bars, to the right and at the bottom of a CAChe document window, to view objects located at the outer edges of the document window or workspace.

Move the scroll bars to the right of a document window by:

- clicking and dragging up and down to view objects above and below the currently displayed objects.

Move the scroll bars at the bottom of a document window by:

- clicking and dragging to the left and right to view objects to the left or right of currently displayed objects.



Refer to *"Using CACHe"*, p 3-17, for a description of how to click and drag using the cursor.

Hiding the scroll bars

You can choose to hide the scroll bars at the right and at the bottom of a CACHe document window.

To hide the scroll bars

1. When the scroll bars are visible, choose **Options | Show Scroll Bars**.

   The scroll bars are no longer displayed at the right and at the bottom of the document window.

   The check mark next to the **Show Scroll Bars** drop-down list option is no longer displayed, indicating that the scroll bars of the workspace are currently hidden.

To redisplay the scroll bars

1. When the scroll bars are hidden, choose **Options | Show Scroll Bars**.

   Scroll bars are displayed at the right and bottom of the active workspace.

   A check mark is displayed next to the **Show Scroll Bars** drop-down list option, indicating that the scroll bars of the workspace are currently visible.

Stereo 3D cursor

If you have a stereo license, the cursor may be drawn in 3D in the workspace.

To display the 3D cursor in the workspace

1. When the cursor exists in 2D in the workspace, choose **Options | 3D Cursor**.

   The cursor is displayed in the workspace in 3D, and a check

mark is displayed next to the 3D Cursor drop-down list option.

To hide the 3D cursor in the workspace

1. When the cursor exists in 3D in the workspace, choose **Options | 3D Cursor**.

   The cursor is displayed in 2D in the workspace, and the check mark next to the 3D Cursor drop-down list option is no longer displayed.

Manipulating document windows

View all open CAChe document windows at the same time using the Windows **Tile** and **Cascade** options. You can also arrange minimized windows using the Windows **Arrange Icons** option.

To arrange windows to overlap in a cascading pattern

1. Choose **Window | Cascade**.

   All open CAChe document windows are opened in a cascading pattern, so that you can view the title bar of each window.

To arrange windows side by side

1. Choose **Window | Tile**.

   All open CAChe document windows are arranged side by side, so that you can view the title bar and a portion of the contents of each window.

To arrange minimized windows

1. Choose **Window | Arrange Icons**.

   All minimized CAChe windows (those made into an icon) are arranged along the bottom of the main CAChe application window.

Using CAChe

The following section explains terms used throughout this User Guide and provides instructions on using the components of the CAChe interface.

Using the mouse

The following terms are used in this User Guide to describe mouse actions.

Select

Select the following items in CAChe:

- dialog box buttons
- check boxes
- radio buttons
- arrow buttons
- directory buttons
- tabs
- workspace tools
- toolbar buttons.

Choose

Choose the following items in CAChe:

- menu options
- drop-down list options.

Click

Click on the following objects:

- document windows to make them active
- in the workspace using the selection tools
- in the workspace using the Atom/Bond tool
- hypertext links in the CAChe Help system.

To click on an object using the selection tools

1. Position the cursor over the workspace object you want to select.
2. Press the left mouse button and release.

   The selected object is highlighted and other workspace objects are grayed out.
3. To select more objects, hold down the **Shift** key.
4. Position the cursor over the next object you want to select, still holding down the **Shift** key.
5. Press the left mouse button and release.

   The second object you selected is highlighted along with the first, while other workspace objects are grayed out.
6. Continue to click on any further objects you want to select, still holding down the **Shift** key.

To click on the workspace using the Atom/Bond tool

1. Position the cursor anywhere over the workspace.
2. Press the left mouse button and release.

   An atom is displayed in the workspace.

Click and drag

Click and drag on the following objects:

- scroll bars in dialog boxes
- sliders in dialog boxes
- in the workspace using the selection tools
- in the workspace using the Atom/Bond tool
- in the workspace using the manipulation tools.

Selection tools

Click and drag in the workspace using the selection tools to draw a selection box around the objects you want to select.

To click and drag using the selection tools

1. Select the selection tool you want to use.
2. Position the cursor to one side of the object or group of objects you want to select.
3. Hold down the left mouse button and drag the cursor to form a selection box around the objects you want to select.

   The selected objects encompassed by the selection box are highlighted, while other workspace objects are grayed out.

Atom/Bond tool

Click and drag in the workspace using the Atom/Bond tool to draw a bond and connecting atom.

To click and drag using the Atom/Bond tool

1. Select the selection tool you want to use.
2. Position the cursor over an atom or bond.
3. Hold down the left mouse button and drag the cursor a short distance across the workspace.
4. A bond and connecting atom are displayed in the workspace, attached to the atom or bond where you started drawing.

Manipulation tools

Click and drag in the workspace using the manipulation tools to move, rotate, and scale objects.

To click and drag using the manipulation tools

1. Select the selection tool you want to use.
2. Position the cursor in the workspace.
3. Hold down the left mouse button and drag the cursor across the workspace.

   The selected object is moved, scaled, or rotated.

Double-click

Double-click on the following items to open them in the Open and Save As dialog box scrolling lists.

- folders
- files.

Using the menu bar

This user guide uses the following convention for choosing options from a menu's drop-down list: **Menu | Drop-down list option**. For example, **File | Save.**

Menu options

You can also perform some menu drop-down list options using either keyboard shortcuts or toolbar buttons.

Refer to *"Toolbar shortcuts"*, p 3-21, for details about toolbar buttons and their equivalent menu options.

Refer to Appendix A, *"Keyboard and Toolbar Shortcuts"*, for a list of keyboard shortcuts that are equivalent to menu options.

Using the toolbar

The following section describes how to use the toolbar buttons.

To select a toolbar button

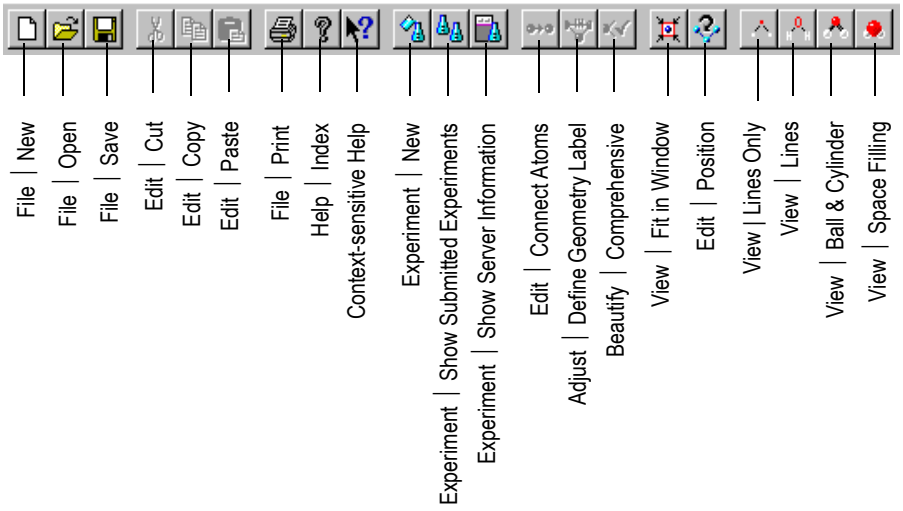
1. Position the cursor over the required button.
2. Press the left mouse button.

   The name of the button appears in the a yellow tool tip box near the cursor and a short description of the function of the button status bar at the bottom of the screen.
3. Release the left mouse button.

   The command to which the toolbar button provides a shortcut is performed.

Toolbar shortcuts

The following diagram shows the menu options that are equivalent to each toolbar button.



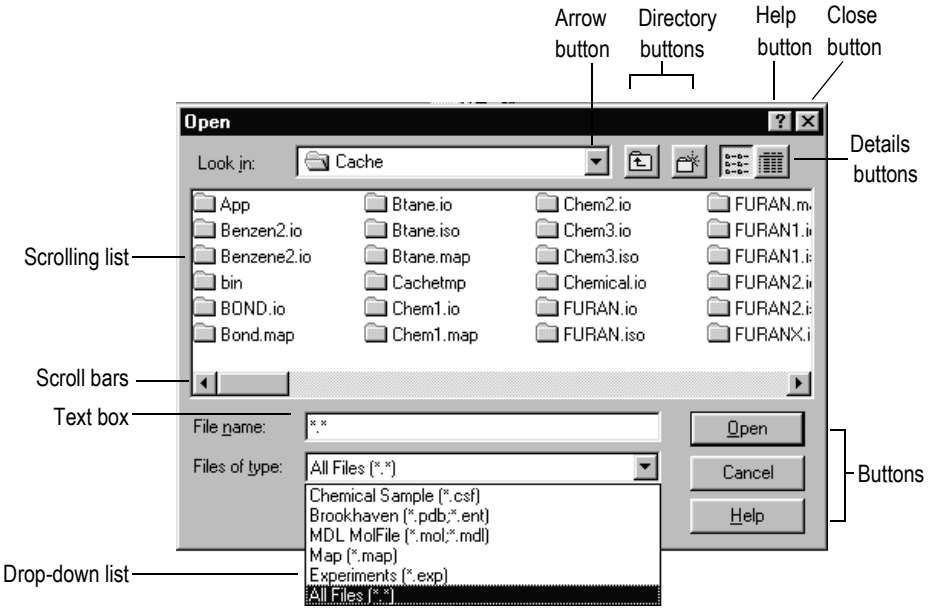
Using dialog boxes

The following section describes how to use the scrolling lists, buttons, and text boxes in a sample CAChe dialog box.

Dialog boxes in CAChe are used to:

- create, open, save, or print files
- change display attributes of objects
- add and define geometry labels and search labels
- change settings for menu options and workspace tools
- initiate experiments
- choose chemical properties on which to base an experiment
- choose procedures used in an experiment
- display experimental results
- display more detailed information about an experimental output file.
- scrolling or non-scrolling lists from which you can select an item
- scrolling or non-scrolling windows that display information.

The following diagram shows examples of the components of a dialog box.



Text boxes

Text boxes allow you to enter information using the keyboard. For example, in the example dialog shown earlier, you can use the **File name** text box to select the existing text, delete it, and type in a new file name.

To enter text into a text box

1. Position the cursor in the required text box and press the left mouse button.

   This activates the text box and fixes the position of the cursor.

2. Type the text you want to add to the text box.

   The text is added at the position of the cursor.

Arrow buttons



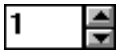
Arrow buttons indicate the presence of a drop-down list. Select an arrow button to display a drop-down list.

To select an arrow button

1. Position the cursor over the arrow button.
2. Press the left mouse button.

   A drop-down list is displayed.

Arrow buttons also indicate a text box in which you can enter a value, or choose a value supplied by selecting either an up or down arrow button at the side of a text box.



To enter a value into a text box using arrow buttons

1. Move the cursor over the up arrow button, if you want to choose a value of `1` or more, or over the down arrow button, if you want to choose a value of `-1` or less.
2. Press the left mouse button.

   The value of `1` or `-1` is displayed in the text box.
3. Increase or decrease the value further by selecting the arrow until the value you require is displayed.

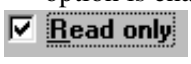
Check boxes

Check boxes can be toggled on and off to enable or disable an option in the dialog box.

To enable a check box

1. Position the cursor over the blank check box.
2. Press the left mouse button.

   A check mark is displayed in the check box to show that the option is enabled.



Radio buttons

Radio buttons can also be toggled on and off to enable or disable an option in the dialog box.

To enable a radio button

1. Position the cursor over the blank radio button.
2. Press the left mouse button.

   A small black circle is displayed in the radio button to show that the option is enabled.



Directory buttons

Directory buttons appear on dialog boxes such as the Open and Save As dialog boxes. The two directory buttons perform the following functions:



- the directory level button, shown to the left, takes you up one directory level to display the contents of the next folder up in your directory structure.



- the new folder button, shown to the left, which creates a new folder within the folder whose contents the dialog box is currently displaying.

To select a directory button

1. Position the cursor over the button you want to select.
2. Press the left mouse button.

   The scrolling list in the dialog box either displays the contents of the next directory up, or a new folder is created in the current directory.

Details buttons

Details buttons appear on some dialog boxes such as the Open and Save As dialog boxes. Toggle between the two details buttons, shown to the left, to view:



- file names only displayed in the dialog box scrolling list.



- file details such as type and size in the dialog box scrolling list.

To select a details button

1. Position the cursor over the button you want to select.
2. Press the left mouse button.

   Files in the scrolling list are either displayed with file name and icon only, or with file name, icon, file type and size, and the date that the file was last modified.

Buttons

Buttons perform an action or display another dialog box containing further options. Examples of buttons are shown below.



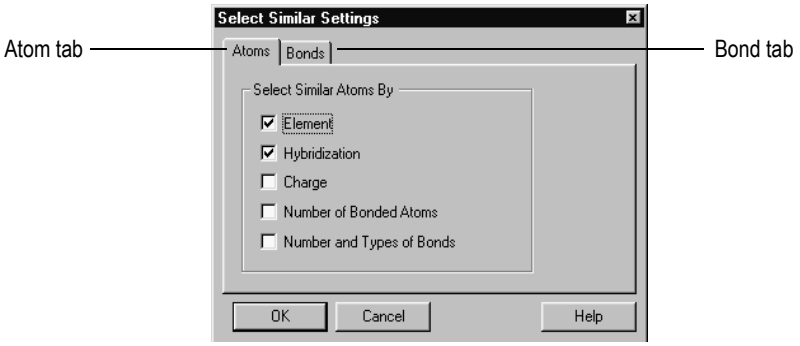
To select a button

1. Position the cursor over the button you want to select.
2. Press the left mouse button.

   An action is performed, or another dialog box is displayed.

Tabs

Tabs display a list of options, radio buttons, or check boxes specific to the object on the tab. A dialog box can contain two or more tabs.



To select a tab

1. Move the cursor over the tab you want to select.
2. Press the left mouse button.

   The selected tab is displayed.

Drop-down lists

Drop-down lists display a number of options. When you choose one, the option you choose is displayed in the relevant text box.

To choose an option from a drop-down list

1. Position the cursor over the drop-down list option you require.
2. Press the left mouse button.

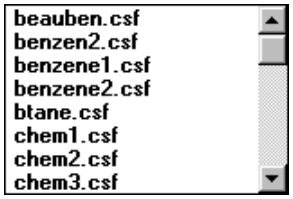
   The drop-down list disappears and the option you chose is displayed in the relevant text box.

Scrolling and non-scrolling lists

Lists can be scrolling or non-scrolling, depending on the number of items being displayed. Lists are used to display items that you:

- select by clicking on the item
- open by double-clicking on the item.

For example, the scrolling list shown below displays a list of files. Select a file by clicking on it.

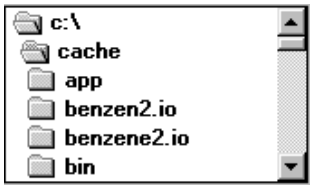


To select an item in a scrolling or non-scrolling list

1. Position the cursor over the item you want to select.
2. Press the left mouse button to select the item.

   The item is highlighted.

The scrolling list shown below displays folders in the `cache` folder on a computer's **C** drive. Open a folder to view the files inside by double-clicking on the folder icon or name.



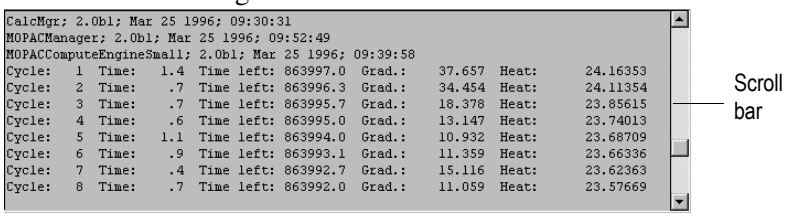
To open an item in a scrolling or non-scrolling list

1. Position the cursor over the item you want to select.
2. Press the left mouse button twice in quick succession to select and open the item at the same time.

   If the item is a folder, the files within that folder are displayed in the dialog box. If the item is a file, the file opens.

Scrolling and non-scrolling windows

Windows display information. Many windows have scroll bars that allow you to view text that has scrolled off the screen. The following window is a scrolling window.



If a window does not display scroll bars, all the information present in that window is currently displayed on screen.

To scroll a window

1. Move the cursor over the square in the scroll bar.
2. Hold down the left mouse button and drag the cursor upwards or downwards to view the window contents above and below the currently displayed information or objects.

Using the workspace selection tools

This section introduces the palette of workspace tools, which is displayed at the left of the workspace window and consists of:

- four selection tools - the Select (default), Select Molecule, Select Similar, and Select Group tool
- a drawing tool - the Atom/Bond tool
- three manipulation tools - the Rotate, Translate, and Scale tool.

This section also describes in detail how to use the default Select tool to do the following:

- select or deselect individual atoms and bonds in the workspace
- select or deselect several atoms and bonds
- select every object in the workspace.

Selecting a tool

To select a tool from the tool palette, click on it. When you select a tool, the cursor changes to represent the selected tool, as shown in the following table.

Workspace tool name	Tool palette icon	Cursor
Select tool (default)		
Select Molecule tool		
Select Similar tool		
Select Group tool		
Atom/Bond tool		
Rotate tool		
Translate tool		
Scale tool		

Introducing the selection tools

Use the selection tools to select workspace objects individually, in groups of similar objects, or molecule by molecule. CAChe allows you to hide atoms, bonds and other objects.

The select tools operate on visible objects. Usually, hidden objects are not selected. A hidden object is selected only if the Select Molecule tool or Select Group tool is used to choose a visible atom or bond and the hidden object is a part of the selected molecule or group.

The Select tool



The Select tool is the default workspace tool. Use it to:

- select one or more visible objects, such as individual atoms or bonds
- deselect one or more objects.
- select all visible objects by clicking on the background



The Select tool and Select cursor are shown to the left.



Refer to *"Using the Select tool"*, p 3-33, for further details.



The Select Molecule tool

Use the Select Molecule tool to:

- select one or more visible molecules
- deselect one or more molecules.



The Select Molecule tool and cursor are shown to the left.



Refer to Chapter 5, *"Modifying Chemical Samples"*, for details about using the Select Molecule tool.



The Select Similar tool.

Use the Select Similar tool to:



- select visible objects of a similar type, for example, all atoms of the same element type, or all bonds of the same bond type
- deselect objects of a similar type.

The Select Similar tool and Select Similar cursor are shown to the left.



Refer to Chapter 5, *"Modifying Chemical Samples"*, for details about using the Select Similar tool, and how to define criteria for similarity.



The Select Group tool

Use the Select Group tool to:



- select a visible atom, and all the atoms with which it shares a group.

The Select Group tool and Select Group cursor are shown to the left.



Refer to Chapter 5, *"Modifying Chemical Samples"*, for details about using the Select Group tool.



The Atom/Bond tool

Use the Atom/Bond tool to:



- draw atoms and bonds.

The Atom/Bond tool and Atom/Bond cursor are shown to the left.



Refer to Chapter 4, *"Creating Chemical Samples"*, for details about using the Atom/Bond tool to draw the constituent atoms and bonds of your molecule.



The Rotate tool:

Use the Rotate tool to:



- rotate objects in two or three dimensions.

The Rotate tool and Rotate cursor are shown to the left.



Refer to Chapter 7, *"Manipulating Molecules"*, for information on how to use the Rotate tool, and how to define the center of rotation for the tool.



The Translate tool

Use the Translate tool to:

- move objects in the workspace in two dimensions.



The Translate tool and Translate cursor are shown to the left.



Refer to Chapter 7, *"Manipulating Molecules"*, for details about using the Translate tool, and how to define the center of rotation for the tool.



The Scale tool.

Use the Scale tool to:

- zoom in on objects



- zoom out from objects.

The Scale tool and Scale cursor are shown to the left.



Refer to Chapter 7, *"Manipulating Molecules"*, for information on how to use the Scale tool.

Using the Select tool



The Select tool is the default workspace tool. Use the Select tool to:

- select one or more workspace objects by clicking on them
- select a group of workspace objects by clicking and dragging around them
- select a group of workspace objects by clicking on them while holding down the **Shift** key
- deselect a selected workspace object by clicking on it

- deselect a group of selected workspace objects by clicking and dragging around them while holding down the **Shift** key
- deselect a group of selected workspace objects by clicking on them while holding down the **Shift** key
- select every visible object in the workspace
- invert the selection by clicking on empty space while holding down the **Shift** key. This has the same effect as **Edit | Invert Selection**.

To select the Select tool

1. Select the Select tool by clicking on it in the tool palette.

   The cursor is displayed as the default arrow cursor or Select tool, shown to the left.



Using the Select tool to select objects

Use the Select tool to select objects by:

- clicking on objects in the workspace
- clicking and dragging around objects in the workspace.

Selecting more than one object

Clicking and dragging is a useful way of selecting more than one object when the objects are close to each other. You can also select more than one object by using the **Shift** key.

To select a group of objects near to each other

1. Position the Select tool to one side of the group of objects you want to select.
2. Press and hold down the left mouse button and drag the Select tool to form a selection box around the objects you want to select.

   The objects are highlighted to show that they are selected.

If the objects you want to select are not close to each other, you can select more than one object by holding down the **Shift** key while you click on subsequent objects.

To select more than one object using the Shift key

1. Position the Select tool over the first object you want to select.
2. Press the left mouse button to select the object.

   The object is highlighted to show that it is selected.
3. Position the Select tool over the second object you want to select.
4. Hold down the **Shift** key and select the second object by clicking on it.

   The second object you selected is highlighted to show that it is selected.
5. Position the Select tool over the third object you want to select.
6. Hold down the **Shift** key and select the third object by clicking on it.

   The third object you selected is highlighted to show it is selected.
7. Continue to hold down the **Shift** key and click on objects until you have selected everything you want.

Using the Select tool to deselect objects

Use the Select tool to deselect objects that are currently selected by:

- clicking on objects in the workspace while holding down the **Shift** key
- clicking and dragging around objects in the workspace while holding down the **Shift** key.

The object is grayed out to show that it is deselected.

Deselecting more than one object

Clicking and dragging around a group of selected objects while holding down the **Shift** key is also a useful way of deselecting more than one object when the objects are close to each other. You can

also deselect more than one object by clicking on each object and holding down the **Shift** key.

To deselect a group of selected objects near to each other

1. Position the Select tool to one side of the group of objects you want to deselect.
2. Hold down the **Shift** key, and click and drag the Select tool to form a selection box around the group of objects you want to deselect.

   The objects are grayed out to show that they are deselected.

   If the objects you want to deselect are not close to each other, you can also deselect more than one object by holding down the **Shift** key while you click on subsequent objects.

To deselect more than one object by clicking

1. Position the Select tool over the object you want to deselect.
2. Hold down the **Shift** key and deselect the object by clicking on it.
3. Position the Select tool over the second object you want to deselect.
4. Hold down the **Shift** key and deselect the second object by clicking on it.

   The second object you deselected is grayed out to show that it is deselected.
5. Position the Select tool over the third object you want to deselect.
6. Hold down the **Shift** key and deselect the third object by clicking on it.

   The third object you deselected is grayed out to show that it is deselected.
7. Continue to hold down the **Shift** key and click on objects until you have deselected everything you want.

Using the Select tool to select every visible object in the workspace

Select everything displayed in the workspace using any of the three selection tools.

To select every visible object in the workspace

1. Select a selection tool by clicking on it.
2. Click in a blank area of the workspace.

   Every visible object in the workspace is highlighted to show that it is selected. Hidden objects are not selected.

Although you can select every object in the workspace, you cannot deselect every object in the workspace. CAChe requires that there is at least one selected object in a workspace or active window.

NOTE The menu command **Edit | Select All** selects all visible and hidden objects.

Using the Select tool to invert the selection in the workspace

Invert the current selection in the workspace using any of the three selection tools.

To invert the visible selection in the workspace

1. Select a selection tool by clicking on it.
2. Do one of the following:
   - Click in a blank area of the workspace.
   - Choose **Edit | Invert Selection**.

   Newly selected objects in the workspace are highlighted to show that they are selected.

NOTE The menu command **Edit | Invert Selection** inverts the selection of both visible and hidden objects.

The Rotate tool



Use the Rotate tool to rotate workspace objects in two and three dimensions around the x, y, and z axes.

To select the Rotate tool



1. Select the Rotate tool by clicking on it in the tool palette.

   The cursor is displayed as the Rotate tool, shown to the left.

Using the Rotate tool

To rotate objects around the z axis

1. Position the Rotate tool outside of the circle that indicates the center of the workspace.
2. Click and drag the Rotate tool.

   All objects in the workspace are rotated around the z axis of the workspace coordinates.

To rotate objects around the x and y axes

1. Position the Rotate tool inside the circle that indicates the center of the workspace.
2. Click and drag the Rotate tool.

   All objects in the workspace are rotated around the y axis if you drag the Rotate tool to the left and right, and around the x axis if you drag the Rotate tool up and down. Dragging the tool diagonally moves objects around the x and y axis.

The Translate tool



Use the Translate tool to move workspace objects in two dimensions.

To select the Translate tool

1. Select the Translate tool by clicking on it in the tool palette.



The cursor is displayed as the Translate tool, shown to the left.

Using the Translate tool

To move objects in two dimensions

1. Position the Translate tool anywhere in the workspace.
2. Click and drag across the workspace.

   All objects in the workspace move in the direction that you dragged the tool.

The Scale tool

Use the Scale tool to:

- zoom in on workspace objects
- zoom out from workspace objects.



To select the Scale tool



1. Select the Scale tool by clicking on it in the tool palette.

   The cursor is displayed as the Scale tool, shown to the left.

Using the Scale tool

To zoom in on objects

1. Position the Scale tool anywhere in the workspace.
2. Click and drag toward the right-hand side or top of the workspace.

   All objects in the workspace are scaled to a larger size.

To zoom out from objects

1. Position the Scale tool anywhere in the workspace.
2. Click and drag toward the left-hand side or bottom of the

workspace.

All objects in the workspace are scaled to a smaller size.

Using the workspace style bar

The workspace style bar consists of four drop-down lists which display settings for:

- element type for an atom
- charge of an atom
- hybridization of an atom
- bond type.

Use the style bar boxes in conjunction with:

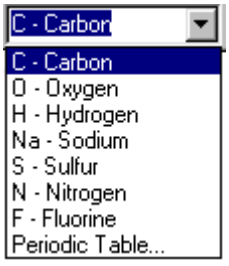
- the Atom/Bond tool
- the selection tools.

Using the style bar with the Atom/Bond tool

Choose atom and bond properties from the style bar's drop-down lists before you draw atoms and bonds using the Atom/Bond tool.

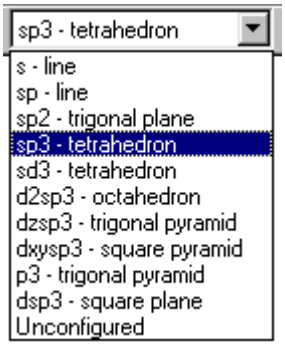
To use the style bar with the Atom/Bond tool

1. Select the arrow button in the Element Type box and choose the element type for the atom that you want to draw from the drop-down list.



2. Select the arrow button in the Hybridization box and choose the hybridization value for the atom that you want to draw from the

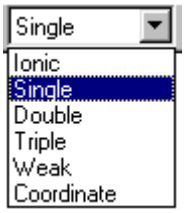
drop-down list.



3. Click in the Charge text box and type the charge for the atom that you want to draw in the Charge text box, or select the up arrow button or down arrow button to display charge values in increasing or decreasing order, respectively.



4. Select the arrow button in the Bond Type box and choose the bond type for the bond that you want to draw from the drop-down list.



5. Use the Atom/Bond tool to draw the atoms and bonds you require.

Refer to Chapter 4, *"Creating Chemical Samples"*, for information on using the Atom/Bond tool.

Using the style bar with the selection tools

Select atoms and bonds with the selection tools to:

- view current atom and bond properties using the style bar boxes

- change atom and bond properties using the style bar boxes.

To view current atom and bond properties

1. Use the Select tool to select the atom or bond whose properties you want to view.

   The current atom or bond properties are displayed in the relevant style bar boxes.

   If you select more than one object and the objects you select possess different properties, the style bar boxes do not display any values.

To change atom or bond properties

1. Use one of the selection tools to select the objects whose values you want to change.

   For example, if you want to change a bond from double to single, select the bond with the Select tool. If you want to change all the atoms in a molecule to another element type, select the molecule with the Select Molecule tool.

   The current value of the object you selected is displayed in the relevant style bar box, if you selected one object, or objects of a similar type.

   No value is displayed in the style bar boxes if you selected more than one object with different properties.

2. Choose the value or property you require from the drop-down list of the relevant style bar box to change the value or property of the selected object.

   For example, choose **single** from the Bond Type drop-down list if you want to change a double bond to a single bond. Choose the new element type from the Element Type drop-down list if you want to change the atoms of a selected molecule to another element type.

   The value or property of the selected object changes to the value or property you chose from the list.

Using CAChe Help

CAChe offers two forms of on-line Help:

- context-sensitive Help, which displays information on any part of the interface, such as a portion of a dialog box, a workspace tool, or a menu option
- the CAChe Help system, accessible from the Contents and Index tabs. Use the tabs to navigate through the Help system to view overview or procedural information on CAChe.

Viewing context-sensitive Help

You can view context-sensitive Help in two ways:

- from the toolbar context-sensitive Help button
- from a dialog box context-sensitive Help button.

Accessing context-sensitive Help from the toolbar

To access context-sensitive Help from the toolbar



1. Select the toolbar button shown to the left.

   The cursor changes to display a question mark, indicating that you are in context-sensitive Help mode.

2. Click on an item in the workspace, or select a menu option or toolbar button.

   A pop-up window is displayed, containing information about the object that you clicked on or the menu option or toolbar button that you selected.

   For example, if you clicked on a tool in the tool palette, the pop-up window contains the tool name and describes the tool's function.

Accessing context-sensitive Help from a dialog box

To access context-sensitive Help from a dialog box



1. Select the Windows query button, shown to the left, located in the top left corner of the dialog box.

   The cursor changes to display a question mark, indicating that you are in context-sensitive Help mode.

2. Click on a radio button, check box, text box, scrolling list, or button in the dialog box.

   A pop-up window is displayed, containing information about the dialog box component that you clicked on.

   For example, if you click on a text box in the dialog box, the pop-up window describes the function of the text box, and the type of information that you type into the text box.

Viewing the CAChe Help system

You can view the CAChe Help system in two ways:

- from the workspace **Help** menu
- from the toolbar Help button.

Accessing the Help system from the Help menu

To access the Help system from the Help menu

1. Choose **Help | CAChe Help Topics** to display the Contents tab.

Accessing the Help system from the toolbar

To access the Help system from the toolbar



1. Select the toolbar button shown to the left to display the Contents tab.

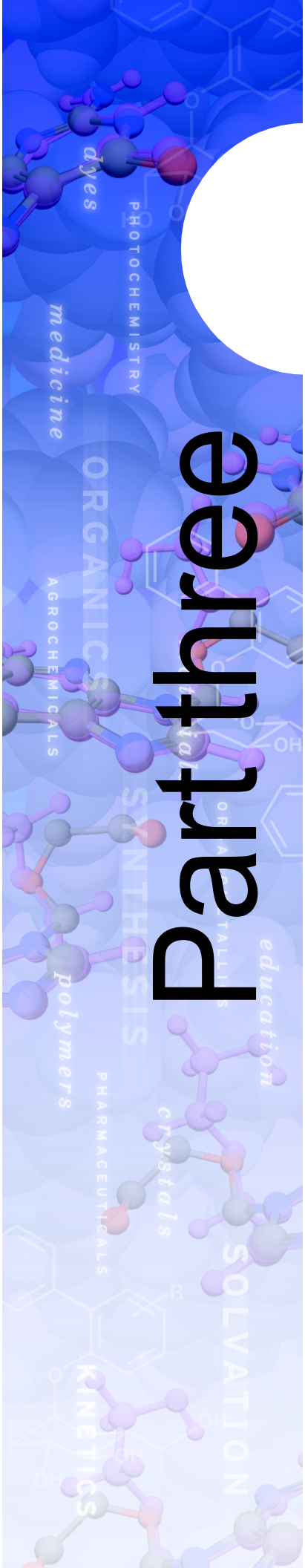
Quitting CAChe

To quit CAChe

1. Choose **File** | **Exit**.

   If you have any unsaved changes in open windows, an alert box asks you if you would like to save changes.

2. Do one of the following:
   - Select **Yes** to save the changes and quit CAChe.
   - Select **No** to quit CAChe without saving the changes.
   - Select **Cancel** to keep CAChe running.



Using CAChe

The following chapters describe how to use CAChe:

Chapter 4, *"Creating Chemical Samples"*.

Chapter 5, *"Modifying Chemical Samples"*.

Chapter 6, *"Viewing Chemical Samples"*.

Chapter 7, *"Manipulating Molecules"*.

Chapter 8, *"Investigating Molecular Geometry"*.

Chapter 9, *"Manipulating Biomolecules"*

Chapter 10, *"Performing Workspace Experiments"*.

Chapter 11, *"Using the Procedure Editor"*

Chapter 12, *"Using ProjectLeader"*.

The following chapters describe details of the different experiments in CAChe:

Chapter 13, *"Optimization and Energy Calculations"*.

Chapter 14, *"Investigating Low-energy Conformations"*.

Chapter 15, *"Investigating Electron Distribution"*.

Chapter 16, *"Investigating Atom and Bond Properties"*.

Chapter 17, *"Investigating Reactions"*.

Chapter 18, *"Investigating Spectra"*.

Chapter 19, *"Investigating Biomolecules"*

4 Creating Chemical Samples

Overview

This chapter explains how to create a molecule using the tools and menu options of the CAChe workspace.

This chapter describes how to:

- draw the atoms and bonds of your molecule in the workspace
- correct the geometry, valence, and hybridization of the resulting structure
- save all CAChe files
- print CAChe files and set up print options for CAChe.

Contents

Working with chemical sample files **4-2**
Opening a new chemical sample file 4-2
Opening an existing chemical sample file 4-3
Drawing a molecule in the workspace **4-4**
Using the Atom/Bond tool 4-4
Drawing an atom 4-5
Drawing a bond 4-6
Completing your molecule **4-9**
Perfecting your molecule **4-10**
Correcting valence 4-10
Defining valence rules 4-10
Correcting hybridization 4-13
Correcting ring geometry 4-13
Correcting geometry 4-14
Correcting hydrogen bond geometry 4-14
The Comprehensive command 4-15
Deleting hydrogens 4-15
Saving files **4-17**
Saving a new file 4-17
Saving an existing file 4-19
Opening a saved file 4-20
Printing files **4-22**
Previewing a printout 4-22
Choosing print options 4-23
Printing a CAChe window 4-25

Working with chemical sample files

You create a molecular structure by drawing atoms and bonds in a document window. The document in which you draw, edit, and save your molecular model is called a chemical sample file, and this is the default file type in CAChe. You use chemical sample files to:

- draw and perfect your molecule
- view your molecule in different ways
- perform experiments on your molecule.

This chapter describes how to draw, edit, view, and save your chemical sample.

Refer to Chapter 10, *"Performing Workspace Experiments"*, for details about launching experiments from a chemical sample file.

Opening a new chemical sample file

When you first start CAChe, a document window entitled `ChemicalSample1` is opened. `ChemicalSample1` is a blank chemical sample file. When you create a molecule in the document window and save the data, the chemical sample file suffix `*.csf` appears in the title bar of the document window.

If you already have a blank `ChemicalSample1` window open, you do not need to open a new chemical sample file.

If you do not have a blank document window currently open, you need to open a new chemical sample file.

To open a new chemical sample file

1. Choose **File** | **New**.

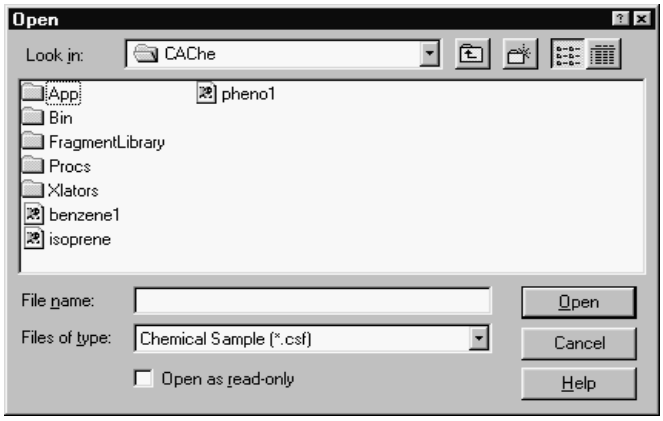
   A blank chemical sample file document window opens.

Opening an existing chemical sample file

Alternatively, you may want to open a chemical sample file that you have already worked on and saved.

To open a saved chemical sample file

1. Choose **File** | **Open** to display the Open dialog box.



2. Select the arrow button in the **Files of type** box to display a drop-down list of file types.
3. Choose **Chemical Sample (*.csf)** from the drop-down list.
4. Select the arrow button in the **Look in** box to display a drop-down list of drives that you can access.
5. Choose the drive where the file that you want to open is located.
6. Click and drag the scroll bar in the scrolling list to display the folder that contains the file that you want to open.
7. Double-click on the folder to open it. A list of files is displayed in the scrolling list.
8. Do one of the following:
   - Click in the **File name** text box and type the file name of the file that you want to open.
   - Click and drag the scroll bar in the scrolling list to locate the file you wish to open, then click on it to select it.
9. Select **Open** to open the chemical sample file.

Drawing a molecule in the workspace

In CAChe, the active chemical sample file window is referred to as the workspace. Each workspace contains a palette of tools which you can use to draw and manipulate your molecule.

Use the Atom/Bond tool to draw the atoms and bonds of your molecule, and use the style bar boxes at the top of the workspace to choose the properties of the atoms and bonds you draw. You can choose these properties either:

- before you draw the atom or bond using the Atom/Bond tool
- after you draw the atom or bond using the selection tools.



Refer to Chapter 5, *"Modifying Chemical Samples"*, for details about using the selection tools to change the atom and bond type on a molecule you have already drawn.

The following section describes how to draw a molecule by:

- choosing atom and bond properties from the style bar
- drawing the atoms and bonds in the workspace using the Atom/Bond tool.



Refer to Chapter 3, *"CAChe Basics"*, for details about using the style bar boxes.

Using the Atom/Bond tool



This section describes how to use the Atom/Bond tool to draw atoms and bonds. Use the Atom/Bond tool to:

- draw an atom by clicking the Atom/Bond tool in the workspace
- draw further bonds and atoms by clicking and dragging the Atom/Bond tool in the workspace
- continue to draw atoms and bonds until your molecule is complete.

To select the Atom/Bond tool

1. Select the Atom/Bond tool by clicking on it in the tool palette.

   The mouse cursor changes to the Atom/Bond tool, shown to the left.

Once you have selected the Atom/Bond tool, you are ready to start drawing the atoms and bonds of your molecule.

Drawing an atom

Drawing an atom involves:

1. Choosing atom properties from the style bar drop-down lists.
2. Clicking in the workspace with the Atom/Bond tool.

NOTE When the Atom/Bond tool is the active tool, clicking anywhere in the workspace draws an atom. The type of atom is determined by the current selections in the style bar's element type, hybridization, and charge drop-down lists.

To draw an atom

1. Select the arrow button in the Element Type box at the left of the style bar.

   A drop-down list of elements is displayed.

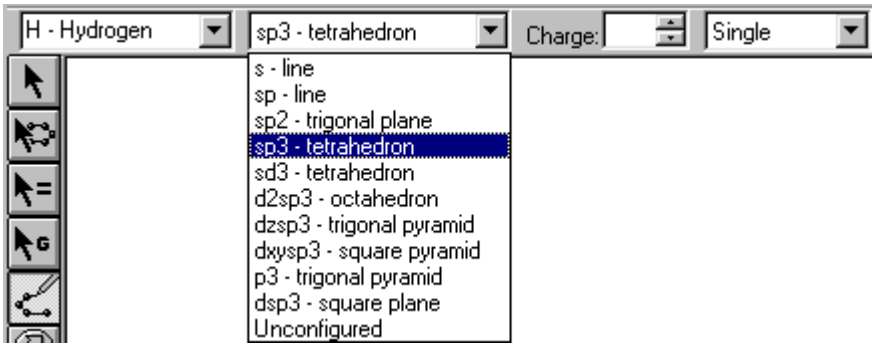


2. Choose an element type from the drop-down list.

   The atom you draw will be of the chosen element type.

3. Select the arrow button in the Hybridization box in the style bar.

   A drop-down list of hybridization options is displayed.



4. Choose a hybridization from the drop-down list.

   The atom you are going to draw will possess hybridization of the chosen value.

5. Do one of the following:

   - Select the up or down arrow button in the Charge text box in the style bar until the positive or negative charge value you require is displayed.
   - Click in the text box and type the charge value you require.





6. Click in the workspace with the Atom/Bond tool.

   An atom of the chosen element type, hybridization, and charge, is displayed, similar to the example shown to the left.

Drawing a bond

When drawing bonds you can either:

- click and drag between two existing atoms to create a bond between the two atoms
- click and drag from an existing atom to a blank part of the workspace to create a bond with an atom attached.

Drawing a bond between two existing atoms

Drawing a bond between existing atoms involves:

1. Choosing a bond type from the style bar Bond Type drop-down list.
2. Positioning the Atom/Bond tool over an existing atom in the workspace.
3. Clicking and dragging to another atom.

The type of bond you draw is determined by the current selection in the style bar's Bond Type drop-down list.

To draw a bond between two existing atoms

1. Select the arrow button in the Bond Type box at the left of the style bar, as shown below:



   A drop-down list of bond types is displayed.

2. Choose a bond type from the drop-down list.

   The bond you are going to draw will be of the chosen bond type.

3. Position the Atom/Bond tool over an atom you have already drawn.
4. Click and drag the Atom/Bond tool across the workspace to another atom you have already drawn.



   A bond of the chosen bond type is displayed between the two atoms. The example to the left shows a single bond between two atoms of the same element.

   If a bond already exists between the two atoms, the next higher order bond type is formed. Bond order cycles through single, double, triple, weak, and back to single bonds when you repeat bond formation.

Drawing a bond with an atom

Drawing a bond with an atom involves:

1. Choosing a bond type from the Bond Type drop-down list in the style bar.
2. Positioning the Atom/Bond tool over an existing atom in the workspace.
3. Clicking and dragging to a blank part of the workspace.

The type of bond you draw is determined by the current selection in the Bond Type drop-down list in the style bar.

To draw a bond between two existing atoms

1. Select the arrow button in the Bond Type box at the left of the style bar, as shown below.



   A drop-down list of bond types is displayed.

2. Choose a bond type from the drop-down list.

   The bond you draw will be of the chosen bond type.

3. Position the Atom/Bond tool over an atom you have already drawn. Click and drag the Atom/Bond tool across the workspace to a blank part of the workspace.

   A bond of the chosen bond type is displayed between the existing atom and a new atom of the currently selected element type. The example to the left shows a single bond between two atoms of different element type.



Completing your molecule

Complete your molecule in one of the following ways:

- continue to draw individual atoms, then join them by drawing bonds between each atom
- continue to draw bonds with an attached atom.

Finish ring structures by completing the last bond you draw over the first atom that was drawn.

When your molecule is complete, you can:

- clean up its structure, geometry, and chemistry
- change selected atoms to another element type, hybridization, and atomic charge
- change selected bonds to another bond type.



Refer to the next section for details about correcting the structure, geometry, and chemistry of your chemical sample.

Refer to Chapter 5, *"Modifying Chemical Samples"*, for details about using the selection tools to change atom and bond properties on a molecule you have already drawn.

Perfecting your molecule

Once you have drawn all the constituent atoms and bonds of your molecule, you can correct its valence, hybridization, and geometry by choosing drop-down list items from the **Beautify** menu.

NOTE Do not use the **Beautify** menu options on any portion of a molecule that has been optimized previously by running an **Optimize Geometry** experiment. This is because the geometry achieved by running an optimization experiment is superior to the geometry resulting from the **Beautify** menu options.



Refer to Chapter 13, *"Optimization and Energy Calculations"*, for information on performing optimization experiments.

Correcting valence

To correct valence

1. Select a workspace selection tool by clicking on it in the tool palette.
2. Using the selection tool, select the portion of your molecule, or the entire molecule, for which you want to correct valence.

   The objects you have selected are highlighted in the workspace.
3. Choose **Beautify** | **Valence**.

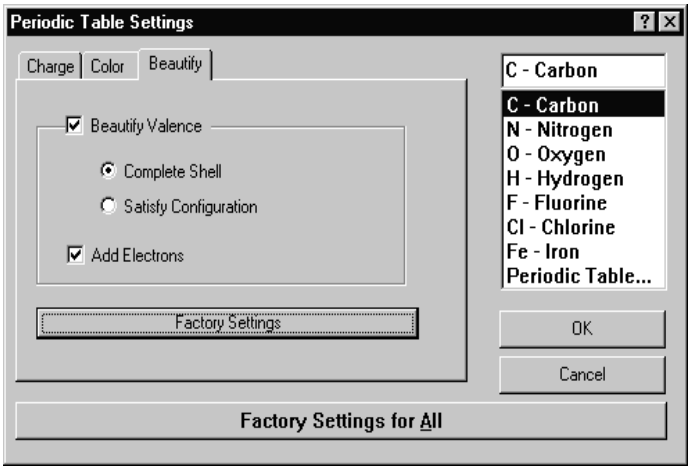
   CAChe adds or removes hydrogen atoms and electrons to or from the selected atoms to satisfy the valence rules for each atom.

Defining valence rules

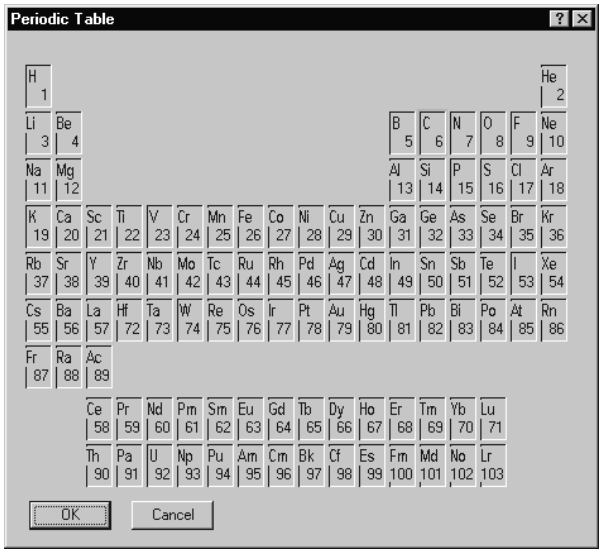
You can change the valence rules that you apply to a chemical sample using the **Beautify** menu options (i.e., **Beautify** | **Valence** and **Beautify** | **Comprehensive**) by changing valence options for each element in the periodic table.

To change the valence rules for an element

1. Choose **Options** | **Periodic Table Settings** to display the Periodic Table Settings dialog box.



2. Do one of the following:
   - Select an element from the element list by clicking on it.
   - If the element you want is not shown, double-click on **Periodic Table** to display the Periodic Table dialog box.



Select the element whose valence rules you want to change by clicking on it. Select **OK** to close the Periodic Table dialog box.

3. Select the **Beautify** tab in the Periodic Table Settings dialog box to display a list of valence options.
4. Select the **Beautify Valence** check box so that it is enabled.

   You can now apply valence rules by using the menu options **Beautify** | **Valence** and **Beautify** | **Comprehensive**.
5. Do one of the following:
   - Select the **Complete Shell** radio button so that it is enabled. You can now fill the valence shell to satisfy atom hybridization by using the menu options **Beautify** | **Valence** and **Beautify** | **Comprehensive**.
   - Select the **Satisfy Configuration** radio button so that it is enabled.
     You can now fill the orbitals of the element's atoms to satisfy atom hybridization by using the menu options **Beautify** | **Valence** and **Beautify** | **Comprehensive**.
6. Select the **Add Electrons** check box so that it is enabled.

   You can now add orbitals to represent non-bonded electrons by using **Beautify** | **Valence** and **Beautify** | **Comprehensive**.
7. Select **OK** to close the Periodic Table Settings dialog box and to save the new valence rules applied by using **Beautify** | **Valence** and **Beautify** | **Comprehensive**.

📖 NOTE Select **Factory Settings** to restore default settings for the application of valence rules for the element currently chosen in the Periodic Table Settings dialog box. **Factory Settings** is displayed when you select the **Beautify** tab.
Select **Factory Settings for All** to restore default settings to all elements for all options selected in the Periodic Table Settings dialog box.

Correcting hybridization

To correct hybridization

1. Select a workspace selection tool by clicking on it in the tool palette.
2. Using the selection tool, select the portion of your molecule, or the entire molecule, for which you want to correct hybridization.

   The objects you have selected are highlighted in the workspace.
3. Choose **Beautify** | **Hybridization**.

   CAChe examines the hybridization (electronic configuration) of each selected atom and bond, and forces the atomic configurations to match the bond types and atom charges, so that electronic configuration is consistent with the number of bonded and non-bonded valence electrons.

   You can label atoms with their hybridization using the Atom Attributes dialog box, accessed by choosing **View** | **Atom Attributes**.

Refer to Chapter 6, *"Viewing Chemical Samples"*, for information about the Atom Attributes dialog box.

Correcting ring geometry

To correct ring geometry

1. Select a workspace selection tool by clicking on it in the tool palette.
2. Using the selection tool, select the portion of your molecule, or the entire molecule, for which you want to correct ring geometry.

   The objects you have selected are highlighted in the workspace.
3. Choose **Beautify** | **Rings**.

   CAChe forces selected cyclic structures into either a planar or puckered conformation, adjusting bond lengths to their proper values.

If the selected structure contains two or more sp^2 atoms, the ring is flattened. If the selected structure contains fused rings, all rings except the first one are flattened.

Correcting geometry

To correct geometry

1. Select a workspace selection tool by clicking on it in the tool palette.
2. Using the selection tool, select the portion of your molecule, or the entire molecule, for which you want to correct geometry.

   The objects you have selected are highlighted in the workspace.
3. Choose **Beautify** | **Geometry**.

   CAChe changes the bond angles and bond lengths in the selected objects to chemically sound values, based on existing atom valence and hybridization.

NOTE This menu option does not clean up ring geometry.

Correcting hydrogen bond geometry

To correct hydrogen bond geometry

1. Select a workspace selection tool by clicking on it in the tool palette.
2. Using the selection tool, select the portion of your molecule, or the entire molecule, for which you want to correct H-bond geometry.
3. The objects you have selected are highlighted in the workspace.Choose **Beautify** | **H-Bonds**.

   CAChe sequentially orients each -OH or -SH hydrogen atom to

maximize hydrogen bonding.

📖 NOTE This menu option moves only hydrogen atoms by rotations and applies to water, hydroxyl or thiol groups only.

The Comprehensive command

The **Beautify** | **Comprehensive** menu option corrects valence, hybridization, geometry, and ring structure in one step. This option is equivalent to choosing **Valence**, **Hybridization**, **Rings**, and **Geometry**, in order, from the **Beautify** menu.

To correct valence, hybridization, ring structure, and geometry in one step

1. Select a workspace selection tool by clicking on it in the tool palette.
2. Using the selection tool, select the portion of your molecule, or the entire molecule, for which you want to correct valence, hybridization, ring structure, and geometry.

   The objects you have selected are highlighted in the workspace.
3. Choose **Beautify** | **Comprehensive**.

   CAChe satisfies the valence and hybridization rules of the selected objects, and corrects the ring structure and geometry.

Deleting hydrogens

The **Beautify** | **Delete Hydrogens** menu option deletes all hydrogen atoms from your structure so you can view or experiment on just the backbone of your chemical sample.

Use the **Beautify** | **Valence** menu option to replace the hydrogen atoms. You can also hide or display hydrogen atoms using the **View** | **Suppress Hydrogens** menu option.

Refer to Chapter 6, *"Viewing Chemical Samples"*, for more information about hiding and displaying hydrogen atoms.

To delete hydrogen atoms

1. Select a workspace selection tool by clicking on it in the tool palette.
2. Using the selection tool, select the portion of your molecule, or the entire molecule, for which you want to correct valence, hybridization, ring structure, and geometry.

   The objects you have selected are highlighted in the workspace.
3. Choose **Beautify | Delete Hydrogens**.

   CAChe deletes all hydrogen atoms in the selected workspace objects.

Saving files

When you save your chemical sample file in CAChe, you save the current orientation of the chemical sample in the workspace and its display style for atoms and bonds chosen from the Atom Attributes and Bond Attributes dialog box options.

The chemical sample is displayed in the same orientation and display style in which you saved the file when you next open it.



Refer to Chapter 6, *"Viewing Chemical Samples"*, for information on the Atom Attributes and Bond Attributes dialog boxes.

You can save all files, of all file types in CAChe, using the menu options described in the next sections, *"Saving a new file"* and *"Saving an existing file"*.

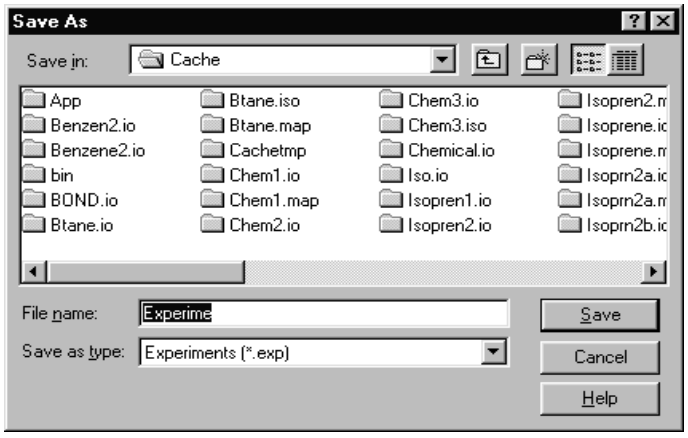
NOTE When you change a new or existing file in CAChe, an asterisk is displayed next to the file name in the workspace title bar to indicate that the file is changed and you need to save it. Once you save the file, the asterisk disappears.

Saving a new file

To save a previously unsaved file

1. Choose **File** | **Save**.

   If this is the first time you are saving the file, the Save As dialog box is displayed.



2. Select the arrow button in the **Save in** box to display a drop-down list of:
   - folders in the directory structure above the currently open folder
   - available drives on which you can save the file.
3. Choose the folder or drive in which you want to save the file from the drop-down list.
4. Do one of the following:



   - To create a new folder in which to save the file, select the dialog box button shown to the left.



   - To move up a level of folders to locate the folder in which you want to save the file, select the dialog box button shown to the left.
   - To save the file in a subfolder, click and drag the scroll bar in the scrolling list to locate the folder in which you want to save the file, and double-click on the folder to open it.
5. Do one of the following:
   - Click in the **File name** text box and type the file name that you want to use to save the file.
   - Click and drag the scroll bar in the scrolling list to display a file that you want to replace, and click on it to select it. That file name is now displayed in the **File name** text box.

6. Select the arrow button in the **Save as type** box and choose the file type you require from the drop-down list.
7. Select **Save** to close the Save As dialog box and to save the file.

Saving an existing file

To save an existing file without changing the name, type, or location

1. Do one of the following:
   - Choose **File** | **Save**.
   - Press **Ctrl S**.
   - Select the toolbar button shown to the left.



   The file is saved.

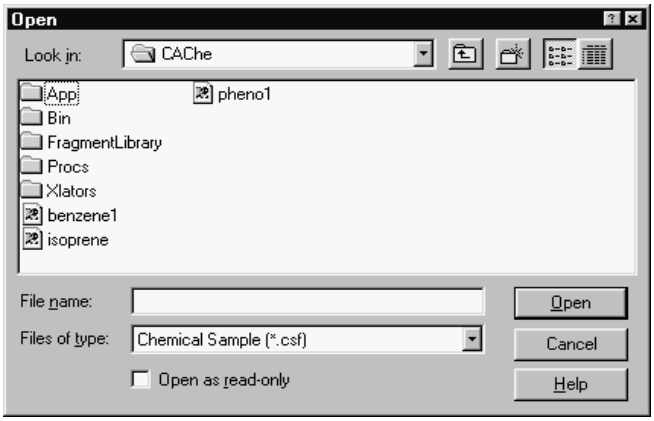
To save an existing file with a new file name, as a different file type, or in a new location

1. Choose **File** | **Save As** to display the Save As dialog box.
2. Do one of the following, as required:
   - Click in the **File name** text box and type the new file name.
   - Select the arrow button in the **Save as type** box and choose the new file type from the drop-down list.
   - Select the arrow button in the **Save in** box and choose from the drop-down list the new drive or folder where you want to save the file.
   - Click and drag the scroll bar in the scrolling list to locate the folder in which you want to save the file, and double-click on the folder to open it.
3. Select **Save** to close the Save As dialog box and to save the file with the new file name, as the different file type, in another folder, or on another drive.

Opening a saved file

To open a saved file

1. Choose **File** | **Open** to display the Open dialog box.



2. Select the arrow button in the **Look in** box to display a drop-down list of:
   - folders in the directory structure above the currently open folder
   - available drives on which you can save the file.
3. Choose the folder or drive where the file is located from the drop-down list.
4. Do one of the following:



   - To move up a level of folders to locate the folder in which you want to save the file, select the dialog box button shown to the left.
   - To save the file in a subfolder, click and drag the scroll bar in the scrolling list to display the folder where the file is located, and double-click on the folder to open it.
5. Select the arrow button in the **Files of type** box and choose the file type of the file that you want to open from the drop-down list.

6. Do one of the following:
   - Click and drag the scroll bar in the scrolling list to locate the file that you want to open, and select the file by clicking on it.
   - Click in the **File name** text box and type the file name of the file that you want to open.
7. Select **Open** to close the Open dialog box and to open the file.

Printing files

CAChe allows you to print a copy of the contents of a workspace. When printing, window contents are scaled so that all currently visible workspace objects are printed. Prints are made as a bitmap at the resolution of your printer.

You can preview and print the contents of all windows in CAChe, regardless of file type.

The following sections describe how to:

- preview a printout
- change print settings
- print a CAChe window.

Previewing a printout

CAChe allows you to view the appearance of a printout before you print.

To preview a printout

1. Activate the document window whose contents you want to preview by clicking on the window.
2. Choose **File** | **Print Preview** to enter print preview mode.

   The contents of the workspace are displayed framed in a page as they would appear in a printout.
3. To zoom into the printout, choose **Zoom In**.

   CAChe zooms into the displayed printout. The cursor changes to the print preview magnifying glass. Click to continue to zoom into the printout in increments.
4. To zoom out from the printout, do one of the following:

   Choose **Zoom Out**.

   CAChe zooms out from the displayed printout in increments.

   Continue to click the print preview cursor until the printout display reverts to its original size.

5. To exit print preview mode, choose **Close**.

   CACHe returns you to the document window.

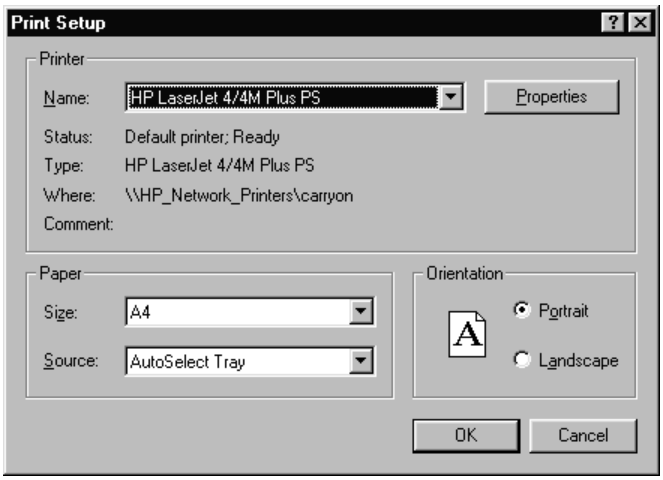
Choosing print options

You can change the following print options in CACHe:

- which printer to use and its properties
- page orientation of a printout
- paper size and source.

To specify a printer and its properties

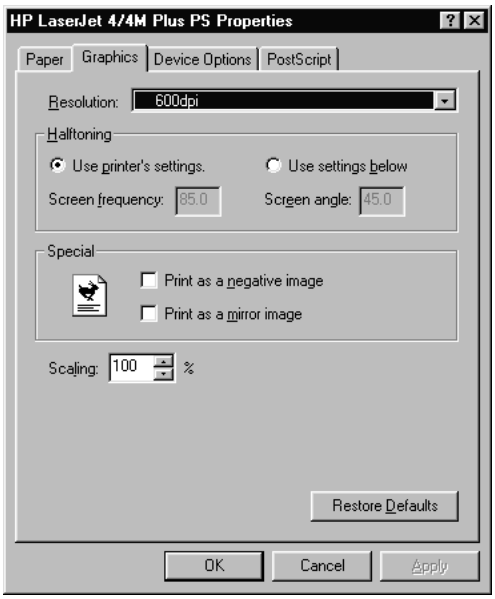
1. Choose **File** | **Print Setup** to display the Print Setup dialog box.



2. To use a different printer from the one displayed in the **Printer** panel, select the arrow button in the **Name** box and choose a printer from the drop-down list.

   The printer's status, type, and location are displayed in the **Printer** panel of the dialog box.

3. To change the properties of the printer, select **Properties** to display a dialog box containing specific options for your printer type.



4. Select the **Paper**, **Graphics**, **Device Options**, or **Postscript** tab to display and select the options relevant to your printer.

NOTE The bitmap created depends on the resolution set for your printer. Therefore, high printer resolution will create a smoother print, but will take longer to print.
Lower printer resolution will be faster to print, and can be useful for very large shaded spheres, e.g., large atoms.

5. Select **OK** to close the dialog box of printer properties and to return to the Print Setup dialog box.
6. Select **OK** in the Print Setup dialog box to save the selected printer and its properties and to close the Print Setup dialog box.

To change page orientation of a printout

1. Choose **File** | **Print Setup** to display the Print Setup dialog box.
2. Select the **Portrait** radio button in the **Orientation** panel to print portrait images, where the paper is longer than it is wider.

3. Select the **Landscape** radio button in the **Orientation** panel to print landscape images, where the paper is wider than it is longer.
4. Select **OK** to save the page orientation and to close the Print Setup dialog box.

To change paper size and source

1. Choose **File** | **Print Setup** to display the Print Setup dialog box.
2. Select the arrow button in the **Size** box, located in the **Paper** panel, and choose a paper size from the drop-down list.
3. Select the arrow button in the **Source** box, located in the **Paper** panel, and choose a paper source from the drop-down list.
4. Select **OK** to save the paper size and source settings, and to close the Print Setup dialog box.

Printing a CAChe window

You can print the contents of all CAChe document windows, regardless of file type. When printing, the contents of a document window are scaled so that all currently visible objects are printed. Prints are made as a bitmap at the resolution of your printer.

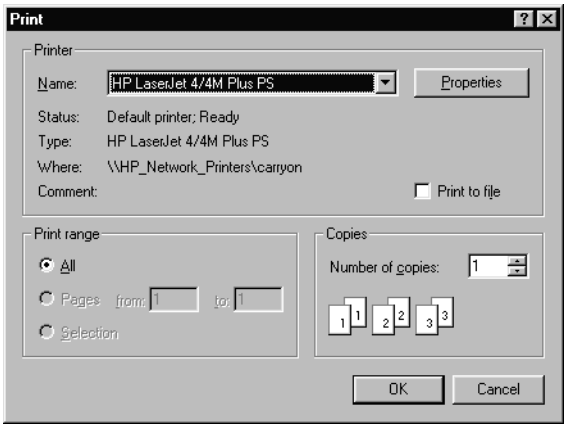
CAChe also gives you the option of printing the contents of a document window to a file, as well as to a printer.

To print a CAChe document window to a printer

1. Activate the document window whose contents you want to print by clicking on the window.
2. Do one of the following:
   - Choose **File** | **Print**
   - Press **Ctrl P**
   - Select the toolbar button shown to the left.



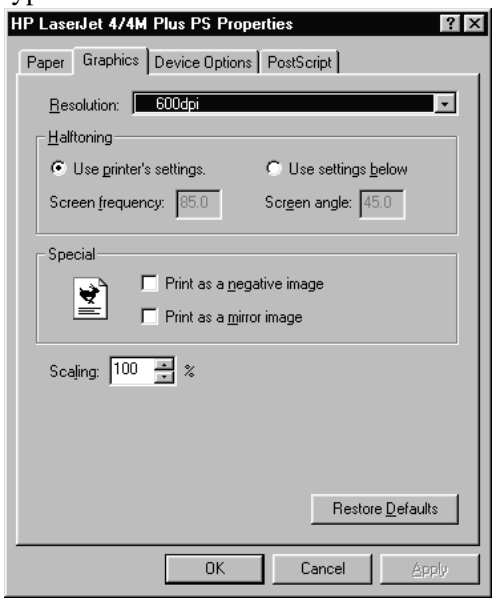
   The Print dialog box is displayed.



3. To use a different printer from the one displayed in the **Printer** panel, select the arrow button in the **Name** box and choose a printer from the drop-down list.

   The printer's status, type, and location are displayed in the **Printer** panel of the dialog box.

4. To change the properties of the printer, select **Properties** to display a dialog box containing specific options for your printer type.



5. Select the **Paper**, **Graphics**, **Device Options**, or **Postscript** tab to display and select the options relevant to your printer.

📖 NOTE The bitmap created depends on the resolution set for your printer. Therefore, high printer resolution will create a smoother print, but will take longer to print. Lower printer resolution will be faster to print, and can be useful for very large shaded spheres, e.g., large atoms.

6. Select **OK** to close the dialog box of printer properties and to return to the Print dialog box.
7. In the **Copies** panel of the Print dialog box, do one of the following:
   - Select the up arrow button in the **Number of Copies** text box to increase the number of copies you require of the printout. Select the down arrow button to decrease the number of copies you require.
   - Click in the **Number of Copies** text box and enter the number of printouts you require.
8. Select **OK** to print the contents of the active document window to a printer and to close the Print dialog box.

📖 TIP If printing is slow, try changing the resolution of your printer, as described in step 5.

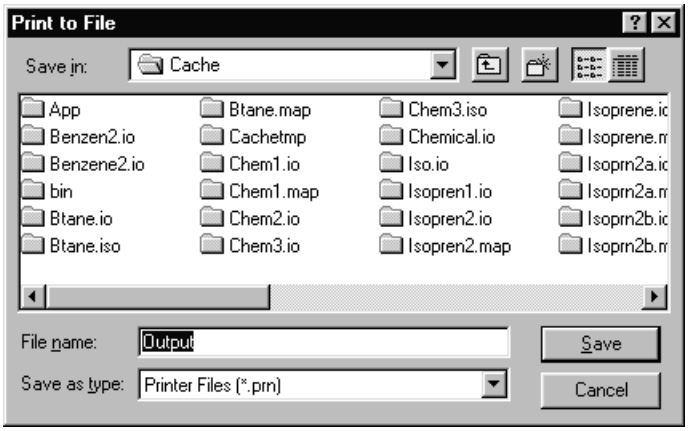
To print a CAChe document window to a file

1. Activate the document window whose contents you want to print to a file by clicking on the window.
2. Do one of the following to display the Print dialog box:
   - Choose **File** | **Print**.
   - Press **Ctrl P**.
   - Select the toolbar button shown to the left.



3. Select the **Print to file** check box so that it is enabled.
4. Select **OK**.

   The Print to File dialog box is displayed.



5. Select the arrow button in the **Save in** box and choose a folder or drive in which to save the file from the drop-down list.
6. Do one of the following:



- To create a new folder in which to save the file, select the dialog box button shown to the left.



- To move up a level of folders to locate the folder in which you want to save the file, select the dialog box button shown to the left.
- To save the file in a subfolder, click and drag the scroll bar in the scrolling list to locate the folder in which you want to save the file, and double-click on the folder to open it.

7. Click in the **File name** text box and enter a name for the file that you are saving.
8. Select the arrow button in the **Save as type** box and choose a file type from the drop-down list for the file that you are saving.
9. Select **Save** to print the contents of the selected document window to a file and to close the Print to File dialog box.

   The image is saved using the file name and file type that you specified, and in the folder you selected.

📖 TIP If printing is slow, try changing the resolution of your printer. Refer to *"Choosing print options"*, p 4-23, for details.

5 Modifying Chemical Samples

Overview

Once you have drawn your molecule, you can change its atom and bond characteristics by selecting atoms and bonds and applying new attributes.

This chapter describes how to:

- use the CAChe workspace selection tools to select portions of your molecule, the entire molecule, or similar workspace objects
- use the CAChe Find command to select portions of your molecule by name or property
- change the atom and bond properties of those selected objects using the workspace style bar
- change the atom and bond properties of those selected objects using the menu options.

Contents

Modifying atoms and bonds **5-2**
Selecting workspace objects **5-3**
The selection tools 5-3
The Select Molecule tool 5-6
The Select Similar tool 5-9
The Select Group tool 5-12
Finding workspace objects 5-14
Selecting neighbors 5-16
Selecting water 5-18
Changing atom and bond properties **5-19**
CAChe bond types 5-32

Modifying atoms and bonds

You can change the components of your molecule and their properties by selecting the objects you want to modify, and choosing the new values or properties from either:

- the style bar boxes at the top of the workspace
- dialog boxes, accessed from the menu, that provide further options for modifying your molecule's atoms and bonds.

Before you can modify the properties of any workspace object, you have to select it with one of the selection tools provided in the tool palette to the left of the workspace.

📖 TIP A quick way to create your molecule is to sketch a chain of atoms and bonds with just one element and bond type. You then select individual atoms and bonds and change their properties using the drop-down lists in the workspace style bar.

Selecting workspace objects

Select workspace objects individually, in groups, or molecule by molecule. Use one of the four selections tools to select what you require in the workspace.

When you select a workspace object, it becomes highlighted in the workspace to show that it is selected, while other objects appear grayed out to show that these objects are deselected.

You can also select workspace objects from the Sample Property Window described in *"Selecting chemical sample data"*, p 6-34 and you can select objects by searching for specific properties using the **Edit | Find** command **Edit | Select Neighbors, Select Locked atoms**.

📖 TIP Objects such as atoms, bonds and labels, can be hidden in one or more views and possibly visible in other views. Hidden objects in one view can be selected using the selection tools in a different view where they are visible. Since commands operate on any selected objects whether hidden or visible, it is important to remember which hidden objects are selected. If you forget which objects are selected, use the command **View | Hide Unselected** to hide all unselected objects and to display any hidden selected objects.

The selection tools

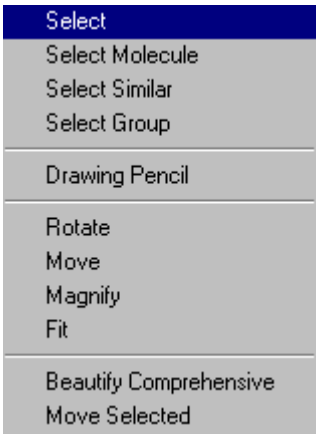
The workspace palette contains four selection tools:

- the Select tool
- the Select Molecule tool
- the Select Similar tool
- the Select Group tool.

Select a tool by clicking on it in the tool palette. As you point at a tool icon with the cursor, the name of the tool appears in a yellow ToolTip and a line of help appears in the lower left border of the window.

When you select a tool, the mouse cursor in the workspace changes shape to indicate which tool is currently selected.

Alternatively, you may choose the tool from the popup menu that appears when you press right mouse button in the 3D Structure Window.



Clicking the right mouse button in the Workspace pops up this menu.

The table below displays the selection tools as they appear in the tool palette, and their corresponding cursors:

Selection tool	Tool palette icon	Mouse cursor
• the Select tool (default)		
• the Select Molecule tool		
• the Select Similar tool		
• the Select Group tool		

General rules for the selection tools

The following methods of selecting and deselecting workspace objects apply to all four selection tools.

Selecting one object

- clicking on an object selects it.

  For example, click on an atom with the Select tool to select the atom, or click on a molecule with the Select Molecule tool to select the molecule. Selecting an atom with the Select Molecule tool will select all the atoms in the molecule, including any hidden atoms.

Selecting more than one object

- clicking and dragging a selection box around objects with the tool selects those objects.

  For example, click and drag around a group of atoms with the Select tool to select all the atoms in the group.

- clicking on one object, then holding down the **Shift** key or holding down the **Ctrl** key while clicking on other objects, selects all those objects.

  For example, to select adjacent atoms, click on one atom, then hold down the **Shift** key and click on the adjacent atom. Continue to hold down the **Shift** key until you have selected everything you want.

- select every visible object in the workspace by clicking anywhere in the workspace with any selection tool. Hidden objects are not selected.

Moving one or more objects in the workspace

- hold the **Alt** key, click and drag on one or more selected objects to move the selected object or objects across the workspace.

Deselecting one object

- clicking on a selected object while holding down either the **Shift** or **Ctrl** key deselects the object.

📖 NOTE You cannot deselect an object if it is the only selected item in the workspace, because CAChe requires that at least one object in the workspace must be selected.

Deselecting more than one object

- clicking on a selected object while holding down either the **Shift** or **Ctrl** key, then clicking on additional selected objects while continuing to hold down the **Shift** or **Ctrl** key, deselects those selected objects.

📖 NOTE You cannot deselect everything in the workspace, because CAChe requires that at least one object must be selected. If you attempt to do this, all objects become selected.

Using the Select tool

Use the Select tool to:

- select one or more objects, such as individual atoms or bonds
- deselect one or more objects.

 Refer to Chapter 3, *"CACche Basics"*, for further details about how to use the Select tool.

The Select Molecule tool



Use the Select Molecule tool to:

- select one or more molecules by clicking on them
- select one or more molecules by clicking and dragging around them
- select a group of molecules by clicking on them while holding down either the **Shift** or **Ctrl** key
- deselect a selected molecule by clicking on it
- deselect a group of selected molecules by clicking and dragging around them while holding down either the **Shift** or **Ctrl** key

- deselect a group of selected molecules by clicking on them while holding down either the **Shift** or **Ctrl** key.

To select the Select Molecule tool

1. Select the Select Molecule tool by clicking on it in the tool palette.



The mouse cursor changes to the Select Molecule tool, shown to the left.

Using the Select Molecule tool to select a molecule

Use the Select Molecule tool to select a molecule by:

- clicking on a molecule in the workspace.

To select a molecule

1. Position the Select Molecule tool over the molecule you want to select.
2. Press the left mouse button to select the molecule.

   The molecule is highlighted to show that it is selected. Hidden atoms in the molecule are selected. To display selected hidden atoms, choose **View | Hide Unselected**.

Using the Select Molecule tool to select more than one molecule

Use the Select Molecule tool to select more than one molecule by:

- clicking on the molecules in the workspace while holding down either the **Shift** or **Ctrl** key
- clicking and dragging around the molecules in the workspace.

To select more than one molecule by clicking

1. Position the Select Molecule tool over the molecule you want to select.
2. Press the left mouse button to select the molecule.

The molecule is highlighted to show that it is selected.

3. Position the Select Molecule tool over the second molecule you want to select.
4. Hold down the either **Shift** or **Ctrl** key and press the left mouse button to select the second molecule.

   The second molecule is highlighted in the workspace to show that it is selected.
5. Continue to hold down either the **Shift** or **Ctrl** key while clicking on molecules until you select all the molecules you require.

To select more than one molecule by clicking and dragging

1. Position the Select Molecule tool to one side of a molecule you want to select.
2. Click and drag the Select Molecule tool to form a selection box around the molecules you want to select.

   The molecules you encompassed in the selection box are highlighted to show that they are selected.

Using the Select Molecule tool to deselect a molecule

To deselect a selected molecule

1. Position the Select Molecule tool over the selected molecule you want to deselect.
2. Press the left mouse button to deselect the molecule.

   The molecule is grayed out to show that it is deselected.

Using the Select Molecule tool to deselect more than one molecule

Use the Select Molecule tool to deselect more than one molecule by:

- holding down either the **Shift** or **Ctrl** key while clicking on the selected molecules
- holding down either the **Shift** or **Ctrl** key and clicking and dragging around the selected molecules in the workspace.

To deselect more than one molecule by clicking

1. Position the Select Molecule tool over the selected molecule you want to deselect and hold down either the **Shift** or **Ctrl** key.
2. Press the left mouse button to deselect the molecule while holding down either the **Shift** or **Ctrl** key.

   The molecule is grayed out to show that it is deselected.
3. Position the Select Molecule tool over the second molecule you want to select.
4. Continue to hold down either the **Shift** or **Ctrl** key and press the left mouse button to select the second molecule.

   The second molecule is grayed out to show that it is deselected.
5. Continue to hold down either the **Shift** or **Ctrl** key while clicking on selected molecules until you deselect all the molecules you require.

To deselect more than one molecule by clicking and dragging

1. Position the Select Molecule tool to one side of a selected molecule you want to deselect.
2. Hold down either the **Shift** or **Ctrl** key and click and drag the Select Molecule tool to form a selection box around the selected molecules you want to deselect.

   The molecules you encompassed in the selection box are grayed out to show that they are deselected.

The Select Similar tool



Use the Select Similar tool to:

- select all atoms or bonds of a similar type
- deselect all atoms or bonds of a similar type.

You can define the criteria for similarity when selecting similar objects with the Select Similar tool by choosing **Options | Select Similar Settings**.

Refer to *"Defining Similarity"*, p 5-11, for details about how to define similarity criteria.

To select the Select Similar tool

1. Select the Select Similar tool by clicking on it in the tool palette.



The mouse cursor changes to the Select Similar tool, shown to the left.

Using the Select Similar tool to select similar atoms or bonds

To select similar atoms

1. Position the Select Similar tool over an atom of the type that you want to select.
2. Press the left mouse button to select the atom and all other atoms of the same type.

   All similar atoms are highlighted in the workspace to show that they are selected.

To select similar bonds

1. Position the Select Similar tool over a bond of the type that you want to select.
2. Press the left mouse button to select the bond and all other bonds of the same type.

   All similar bonds are highlighted in the workspace to show that they are selected.

Using the Select Similar tools to deselect similar atoms or bonds

To deselect similar atoms

1. Position the Select Similar tool over a selected atom of the type that you want to deselect.
2. Hold down either the **Shift** or **Ctrl** key and press the left mouse button to deselect the atom and all other atoms of the same type.

   All similar atoms are grayed out in the workspace to show that they are deselected.

To deselect similar bonds

1. Position the Select Similar tool over a selected bond of the type that you want to deselect.
2. Hold down either the **Shift** or **Ctrl** key and press the left mouse button to select the bond and all other bonds of the same type.

   All similar bonds are highlighted in the workspace to show that they are selected.

Defining Similarity

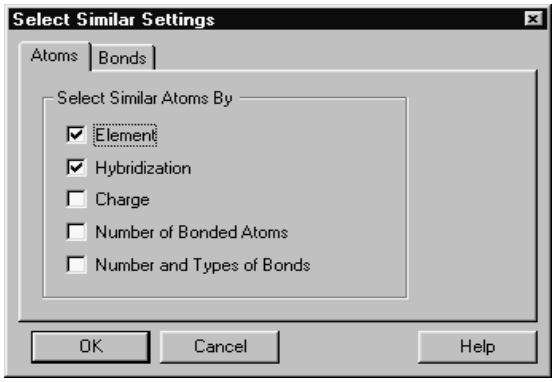
You can define the following criteria for selecting similar atoms:

- element type
- hybridization
- charge
- number of bonded atoms
- number and type of bonds.

You can define the following criteria for selecting similar bonds:

- bond type
- element of bonded atoms.

To do this, you use the Select Similar Settings dialog box.



To define similarity criteria for the Select Similar tool

1. Choose **Options** | **Select Similar Settings**.

   The Select Similar Settings dialog box is displayed.
2. Select the **Atoms** tab to display a list of atom property check boxes.
3. Select the required check boxes so that they are enabled.
4. Select the **Bonds** tab to display a list of bond property check boxes.
5. Select the required check boxes so that they are enabled.
6. Select **OK** to close the Select Similar Settings dialog box.

The Select Group tool



Use the workspace's Select Group tool to:

- select an atom and all the atoms with which it shares a group
- deselect an atom and all atoms in the group
- select an RMS label.
- select bonds in a group

To select the Select Group tool



1. Select the Select Group tool by clicking on it in the tool palette.

   The mouse cursor changes to the Select Group tool, shown to the left.

Using the Select Group tool to select a group

To select a group

1. In the workspace, select the Select tool, and do one of the following:
   - position the cursor to one side of the group you want to select, hold down the **left** mouse button and drag the cursor to form a selection box around the group.
   - select an atom, and hold down either the **Shift** or **Ctrl** key while you select each of the remaining atoms in the group by clicking on it.

   The atoms are highlighted to show they are selected.
2. Choose **Edit | Group Atoms** to display the Group Atoms dialog box.
3. Enter a name for the group of selected atoms in the **Group Name** text box.
4. Select **>>Group>>** to display the new group in the **Defined Groups** list.
5. Select **OK** to close the Group Atoms dialog box.
6. Select the Select Group tool, and select an atom in the defined group.

   All the atoms that share a group with this atom are selected, even hidden atoms.

To deselect a group

1. In the workspace, position the Select Group tool over the selected group you want to deselect.
2. Press the **left** mouse button to deselect the group.

   The group is grayed out to show that it is deselected.

Using the Select Group tool to select an RMS error label

To select an RMS error label

1. From two molecules in the workspace, select a corresponding atom from each, both of which are defined within a group.
2. Choose **Analyze | Calculate RMS Error** to display an RMS error label.
3. Use the Select Group tool to select the RMS error label.

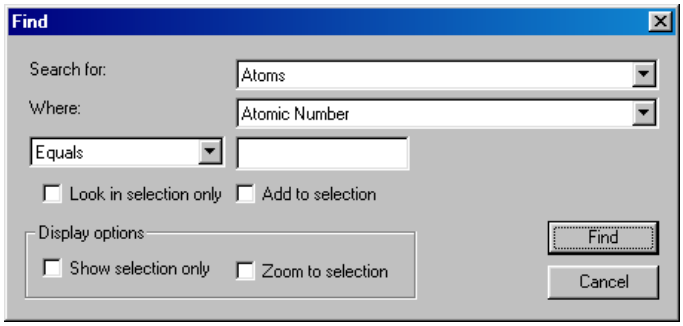
   The atoms in the groups, used for the calculation, are selected.

Finding workspace objects

Select chemical sample atoms, bonds and groups by property using the Find menu item.

To find objects with specific properties

1. From either the workspace or the Sample Properties view choose **Edit | Find** to display the Find dialog box.



2. Choose the atoms, bonds or groups from the **Search for** drop-down menu.
3. Choose the property from the **Where** drop-down menu. The properties listed are those available in the chemical sample for the chosen object. They are listed in alphabetic order. Different molecules may have different properties available for searching.

4. Choose the search criteria. The criteria in the list depend upon the type of property. Criteria available for strings, names, integers and real numbers are different.

   Strings: *Is, Is not, Contains, Does not contain*
   Names: *Is, Is not*
   Integers: *Equals, Not equals, Is less than, Is more than, Is in range, Is not in range*
   Real numbers: *Equals (+-), Is less than, Is more than, Is in range, Is not in range*

5. Type the criteria values in the text box. Range criteria (e.g. "**Is in Range** or **Equals +-**) display two text boxes to specify the range.

   When entering a range, enter the lower and upper values.

   When comparing real numbers equality, enter the value you are searching for and the interval that defines equality.

6. (optional) Check **Look in selection only** to restrict the search to the currently selected objects.

📖 TIP To find objects that match search criteria for one property AND a different property, use the Find command twice. On the second use check **Look in selection only** to find objects that match the search criteria for the first property and the second property.

7. (optional) Check **Add to selection** if you want to extend the current selection with the newly selected items.

📖 TIP To find objects that match search criteria for one property OR a different property, use the Find command twice. On the second use check **Add to selection** to find objects that match the search criteria for the first property or the second property.

8. Check **Show selection only** to hide all objects that are not selected.
9. Check **Zoom to selection** to fit the selected objects in the workspace once they are found. This option is grayed unless the Find command was invoked from a workspace.
10. Click **Cancel** to exit without changing the current selection.

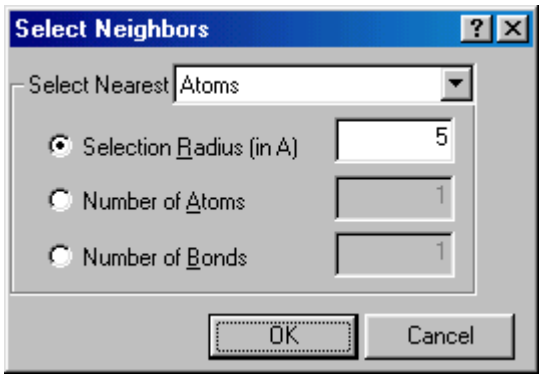
The selected objects are highlighted.

Selecting neighbors

Using the Select tool in the workspace to select atoms or bonds adjacent to selected atoms in large molecules is tedious and error prone. CAChe provides a single command that selects atoms and bonds that neighbor selected atoms.

To select neighboring atoms

1. From the workspace choose **Edit | Select Neighbors**. The following dialog appears:



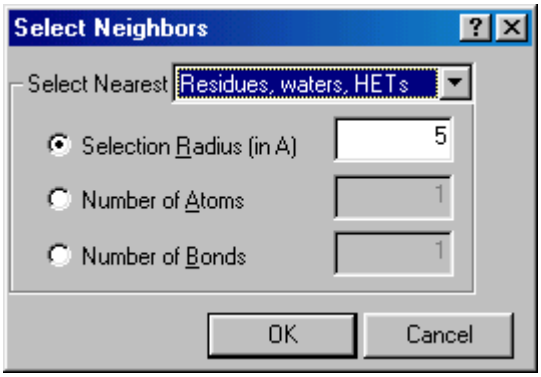
2. Choose the method to **Select Nearest** by
   - Selection Radius
   - Number of Atoms
   - Number of Bonds
3. Type the radius, number of atoms or number of bonds in the box adjacent to the chosen method.
4. Click **OK** to select the all neighboring atoms and add them to the current selection.

   When selecting neighboring atoms by number of atoms, CAChe creates a list of the atoms closest to the currently selected atoms and orders that list by distance from the selection. CAChe then adds the nearest specified number of atoms to the current selection.

When selecting by number of neighboring bonds, CAChe selects all atoms that are closer than the specified number of bonds from the currently selected atoms.

To select neighboring residues, waters and HET groups

1. From the workspace choose **Edit | Select Neighbors**. The Select Neighbors dialog appears.
2. Choose **Residues, waters, HETs** from the **Select Nearest** pull down menu.



3. Choose the method to **Select Nearest** by
   - Selection Radius
   - Number of Atoms
   - Number of Bonds
4. Type the radius, number of atoms or number of bonds in the box adjacent to the chosen method.
5. Click **OK** to select the all neighboring residues, waters and HETs and add them to the current selection.

   When selecting neighboring residues, waters and HETs by number of atoms, CAChe creates a list of the atoms closest to the currently selected atoms and orders that list by distance from the selection. CAChe then adds the nearest specified number of atoms to the current selection.

   When selecting by number of neighboring bonds, CAChe selects

all residues, waters and HETs that are closer than the specified number of bonds from the currently selected atoms.

Selecting water

Using the Select tool in the workspace to select all water molecules in a protein crystal or solvated chemical sample is tedious and error prone. CAChe provides a single command that selects all water molecules.

To select all water molecules

1. Choose **Edit | Select Water**.

   All hidden or visible water molecules are selected.

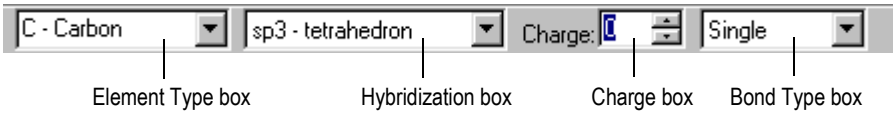
Changing atom and bond properties

Once you have selected the atom, bond, or molecule that you want to change, you choose its new values or properties from:

- the style bar boxes at the top of the workspace
- dialog boxes, accessed from the menu, that provide further options for modifying your molecule's atoms and bonds
- **Beautify** menu options that correct an atom's hybridization
- an **Edit** menu option that changes bond type while connecting two atoms participating in the bond.

Changing an atom using the style bar

The quickest way to change the element type, hybridization, or charge of an atom involves using the Element Type, Hybridization, and Charge style bar boxes at the top of the workspace.



To change an atom's element type using the style bar boxes

1. Select the atom or group of atoms whose element type you want to change by clicking on the atoms with a selection tool.

   The atom or group of atoms are highlighted to show that they are selected.

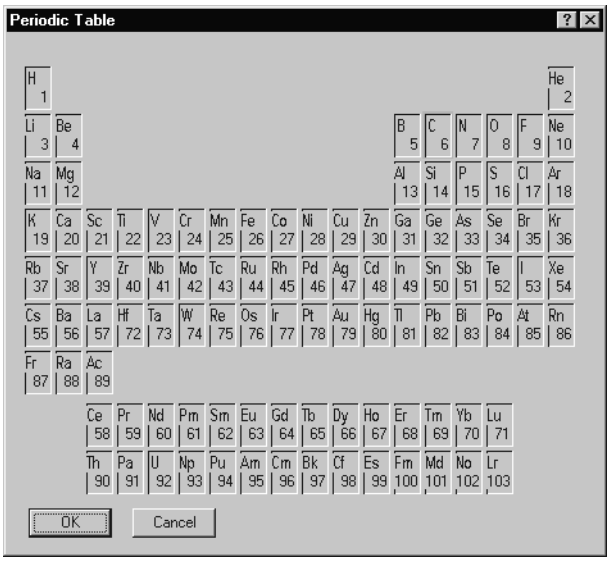
2. Select the arrow button in the Element Type box.

   A drop-down list is displayed, listing the last seven element types you have used.

3. If the element you require is displayed, choose it from the drop-down list.

   The element is displayed in the Element Type box and the selected atom, or group of atoms, changes to the chosen element type.

4. If the element you require is not displayed, choose **Periodic Table** from the drop-down list to display the Periodic Table dialog box.



5. Select an element by double-clicking on it, or clicking on it and selecting **OK**.

   The Periodic Table dialog box closes. The element you have chosen is displayed in the Element Type box and the selected atom changes to the chosen element type.

To change hybridization of an atom using the style bar

1. Select the atom or group of atoms whose hybridization you want to change by clicking on the atoms with a selection tool.

   The atom or group of atoms are highlighted to show that they are selected.

2. Select the arrow button in the Hybridization box.

   A drop-down list is displayed, listing a number of hybridization options.

3. Choose the hybridization you require from the drop-down list.

   The hybridization is displayed in the Hybridization box and the selected atom changes to the chosen hybridization value.

To change the charge of an atom using the style bar

1. Select the atom or group of atoms whose charge you want to change by clicking on the atoms with a selection tool.

   The atom or group of atoms are highlighted to show that they are selected.

2. Select the up or down arrow button in the Charge text box to display the positive or negative value you require, or enter the value you require by clicking in the text box.

   The charge of the selected atom changes to the positive or negative value that you selected or entered into the Charge text box.

Changing an atom using the Atom Attributes dialog box

You can also change the element type, hybridization, and charge of an atom using the Atom Attributes dialog box. The dialog box also provides access to display options that you can apply to one or more selected atoms.



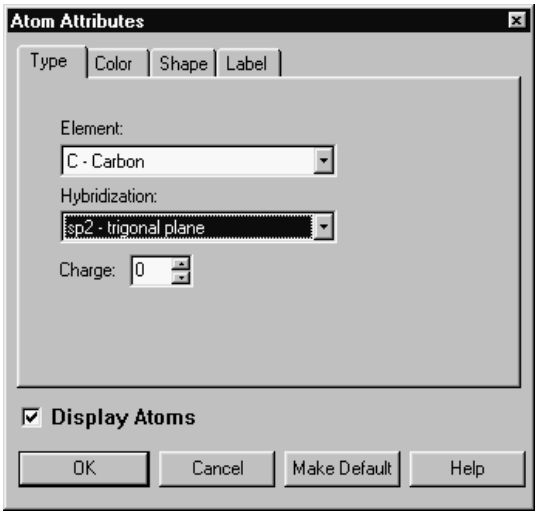
Refer to Chapter 6, *"Viewing Chemical Samples"*, for details about changing the appearance of an atom.

To change an atom's element type, hybridization, and charge using the Atom Attributes dialog box

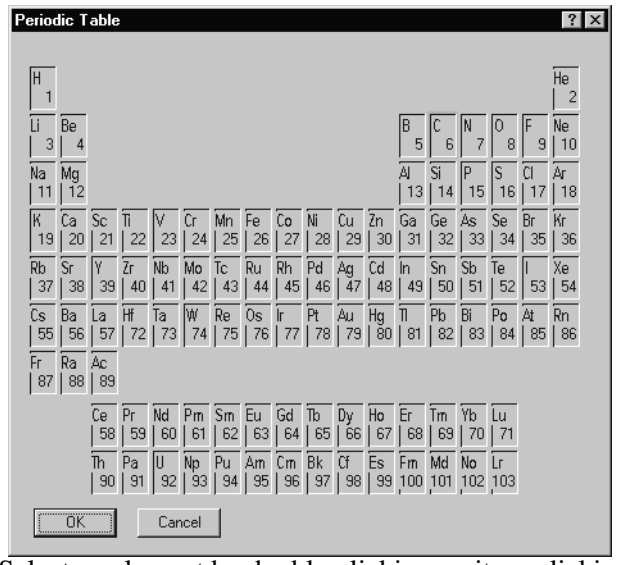
1. Select the atom or group of atoms whose element type, hybridization, or charge you want to change by clicking on the atoms with a selection tool.

   The atom or group of atoms are highlighted to show that they are selected.

2. Choose **View** | **Atom Attributes** to display the Atom Attributes dialog box.



3. Select the **Type** tab to display the **Element**, **Hybridization** and **Charge** boxes.
4. Select the arrow button in the **Element** box to display a drop-down list which is identical to the Element Type drop-down list in the style bar.
5. Select the element you require from the drop-down list, if the element is displayed.
6. If the element you require is not displayed, choose **Periodic Table** from the drop-down list to display the Periodic Table dialog box.



7. Select an element by double-clicking on it, or clicking on it and selecting **OK**.

   The Periodic Table dialog box closes and the element you have chosen is displayed in the **Element** box in the Atom Attributes dialog box.

8. Select the arrow button in the **Hybridization** box and choose the hybridization you require from the drop-down list.

9. Do one of the following:

   - Select the up or down arrow button in the **Charge** text box to display the positive or negative atomic charge you require.
   - Click in the text box and enter the atomic charge you require.

10. Select **OK** to close the Atom Attributes dialog box.

    The selected atom or group of atoms changes to the element type, hybridization, and positive or negative atomic charge that you have chosen in the Atom Attributes dialog box.

Changing an atom's hybridization using the Beautify menu

Another way to change an atom's hybridization is to select the atom and choose **Beautify** | **Hybridization**, or **Beautify** | **Comprehensive**.

Both these menu options employ valence rules to change atomic hybridization to match the existing bond type and atomic charge.

However, because the valence of the atoms must be satisfied before you change hybridization, **Beautify** | **Comprehensive** is the best menu option to use if there is unsatisfied valence in your sample. **Beautify** | **Comprehensive** corrects the valence, hybridization, ring structure, and geometry of your sample in one step.



Refer to Chapter 4, *"Creating Chemical Samples"*, for more information on the **Beautify** menu.



To change an atom's hybridization using the Beautify menu

1. Select the atom or group of atoms whose hybridization you want to change by clicking on the atoms with a selection tool.

   The atom or group of atoms are highlighted to show that they are selected.

2. Do one of the following:

   - Choose **Beautify** | **Comprehensive** if there is unsatisfied valence in your sample.
   - Choose **Beautify** | **Hybridization** if you have already satisfied the valence rules for your sample.

   CAChe changes the atomic hybridization of the selected atom or group of atoms to match bond type and atomic charge.

Checking an atom's hybridization using the Beautify menu

A way to check atom hybridizations is to select the atoms and choose **Beautify | Check Hybridization**.

This menu option employs valence rules to check atomic hybridization to match the existing bond type and atomic charge.



Refer to Chapter 4, *"Creating Chemical Samples"*, for more information on the **Beautify** menu.



To check an atom's hybridization using the Beautify menu

1. Select the atom or group of atoms whose hybridization you want to change by clicking on the atoms with a selection tool.

   The atom or group of atoms are highlighted to show that they are selected.

2. Choose **Beautify | Check Hybridization**.

   CAChe checks the atomic hybridization of the selected atom or group of atoms to match bond type and atomic charge. If the hybridization is correct, CAChe displays a dialog with the message "**Hybridization OK**". Otherwise, CAChe highlights the atoms which do not satisfy the hybridization rules. Choose **Beautify | Hybridization** to correct the hybridization of the selected atoms.

Checking an atom's valence using the Beautify menu

A way to check atom valences is to select the atoms and choose **Beautify | Check Valence**.

This menu option employs valence rules to check atomic valence to match the existing bond type and atomic charge.



Refer to Chapter 4, *"Creating Chemical Samples"*, for more information on the **Beautify** menu.

To check an atom's valence using the Beautify menu

1. Select the atom or group of atoms whose valence you want to change by clicking on the atoms with a selection tool.

   The atom or group of atoms are highlighted to show that they are selected.

2. Choose **Beautify | Check Valence**.
3. CAChe checks the atomic valence of the selected atom or group of atoms to match bond type and atomic charge. If the valence is correct, CAChe displays a dialog with the message "**Valence OK**". Otherwise, CAChe highlights the atoms which do not satisfy the valence rules. Choose **Beautify | Valence** to correct the valence of the selected atoms.

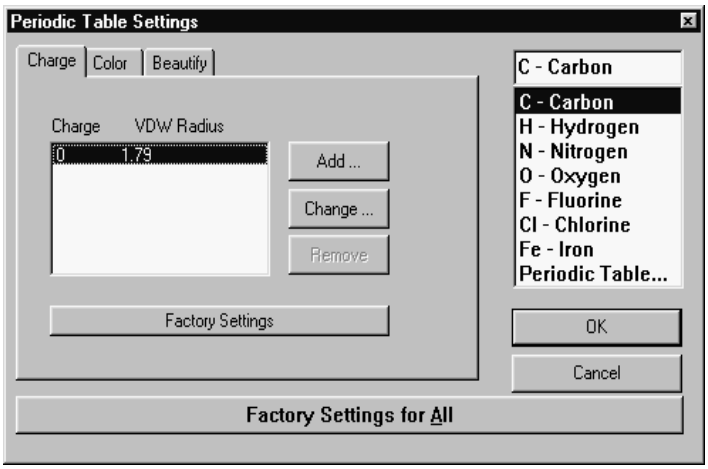
Changing an atom's radius for a particular atomic charge

You can specify atomic radius for a particular atomic charge for any element in the periodic table.

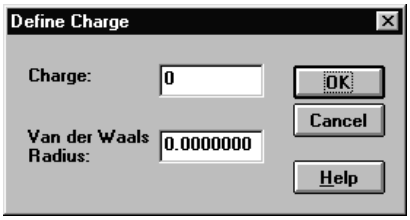
To specify atomic radius for a particular atomic charge

1. Choose **Options | Periodic Table Settings** to display the

Periodic Table Settings dialog box.



2. Do one of the following:
   - Choose the element for which you want to specify a radius associated with atomic charge from the element list by clicking on it.
   - If the element you require is not shown in the list, double-click on Periodic Table to display the Periodic Table dialog box.
3. Select the **Charge** tab to display the **Charge/VDW Radius** list.
4. To add a new list item, select **Add** to display the Define Charge dialog box.



5. Click in the **Charge** text box and type a value for atomic charge.
6. Click in the **Van der Waals Radius** text box and type a value for atomic radius.
7. Select **OK** to close the Define Charge dialog box.

   The charge and van der Waals radius values are displayed in the **Charge/VDW Radius** list in the Periodic Table Settings dialog

box.

8. To change an existing list item, select the list item containing the atomic charge and radius values you want to change, and select **Change** to display the Define Charge dialog box.
9. Click in the **Charge** or **Van der Waals Radius** text box and type a new value for atomic charge or radius.
10. Select **OK** to close the Define Charge dialog box.

    The new charge and van der Waals radius values are displayed in the **Charge/VDW Radius** list in the Periodic Table Settings dialog box.
11. To remove an existing list item, select the list item containing the atomic charge and radius values you want to remove, and select **Remove**.

    The list item disappears from the list.
12. To apply a radius value to a specific atomic charge for the currently selected element, select the list item containing the charge and corresponding radius values that you require.
13. Select **OK** to close the Periodic Table Settings dialog box.

    All atoms of the element you chose, with the atomic charge you specified, are displayed in the workspace with the radius you specified. The radius value applies to all new atoms of that element that you draw which possess the atomic charge you specified, and all atoms in saved chemical sample files with the atomic charge you specified.

Changing a bond using the style bar

Change the bond type of a selected bond using the Bond Type box in the style bar at the top of the workspace.



To change bond type using the Bond Type style bar box

1. Select the bond or group of bonds whose bond type you want to change by clicking on the bonds with a selection tool.

The bond, or group of bonds, are highlighted to show that they are selected.

2. Select the arrow button in the Bond Type box to the right of the style bar.

   A drop-down list of bond types is displayed.

3. Choose the bond type you require from the drop-down list.

   The bond type you have chosen is displayed in the Bond Type box, and the selected bond changes to the bond type you have chosen.

Changing a bond using the Bond Attributes dialog box

You can also change a bond's type using the Bond Attributes dialog box. The dialog box also provides access to display options that you can apply to one or more selected bonds.



Refer to Chapter 6, *"Viewing Chemical Samples"*, for details about changing the appearance of a bond.

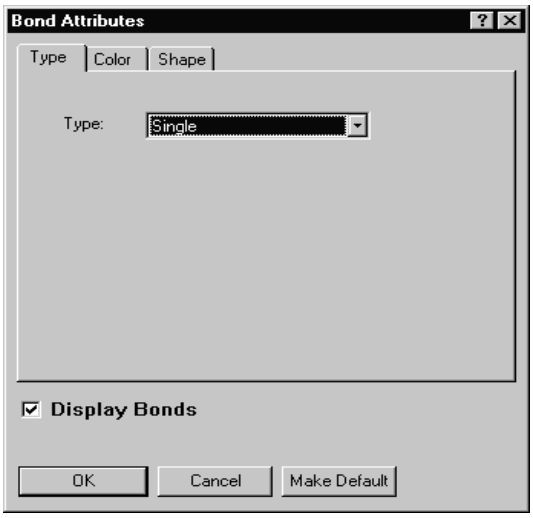


To change bond type using the Bond Attributes dialog box

1. Select the bond, or group of bonds, whose type you want to change by clicking on the bonds with a selection tool.

   The bond, or group of bonds, are highlighted to show that they are selected.

2. Choose **View** | **Bond Attributes** to display the Bond Attributes dialog box.



3. Select the **Type** tab to display the **Type** box.
4. Select the arrow button in the **Type** box to display a drop-down list which is identical to the Bond Type drop-down list in the style bar.
5. Select the bond type you require from the drop-down list.
6. Select **OK** to close the Bond Attributes dialog box.

   The selected bond or group of bonds changes to the bond type that you have chosen in the Bond Attributes dialog box.

Changing bond type while connecting atoms

Another way to change bond type is to select the two atoms participating in the bond, and connect the atoms using the **Edit | Connect Atoms** menu option. The connecting bond cycles through the following bond types every time you choose this menu option:

- single
- double
- triple
- weak.

To change bond type while connecting atoms

1. Select the two atoms participating in the bond by clicking on the first atom with the Select tool, then holding down the **Shift** key and clicking on the second atom with the Select tool.

   The atoms are highlighted to show that they are selected.

2. Do one of the following:

   - Choose **Edit | Connect Atoms**.
   - Press **Ctrl K**.
   - Select the Connect Atoms toolbar button, shown to the left.

   The selected bond changes to one of the following bond types: single, double, triple, or weak.

3. Do one of the following:

   - Continue to choose **Edit | Connect Atoms.**
   - Continue to press **Ctrl K**.
   - Continue to select the Connect Atoms toolbar button, until the selected bond changes to the bond type you require.

Reversing a coordinate bond

CAChe enables you to reverse the direction of a coordinate bond.

To reverse a coordinate bond

1. Select the molecule that contains the coordinate bond(s) by clicking on the molecule with the Select Molecule tool.

   The molecule is highlighted to show that it is selected.

2. Choose **Edit | Reverse Coordinate Bonds**.

   The coordinate bond(s) are reversed.

CAChe bond types

CAChe recognizes the following seven types of bonds:

- single covalent bonds
- double covalent bonds
- triple covalent bonds
- weak bonds
- ionic bonds
- coordinate covalent bonds (dative bonds)
- π coordination bonds.

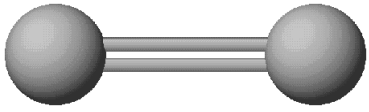
Single covalent bonds

Single covalent bonds share two electrons between two atoms, in a single bond created by the overlap of one orbital from each bonded atom. Each atom contributes one of its valence electrons to the bond. The following example shows a single covalent bond displayed as a cylinder.



Double covalent bonds

Double covalent bonds share four electrons between two atoms, in two bonds created by the overlap of two orbitals on each atom. Each atom contributes two of its valence electrons to the bond. The following example shows a double covalent bond displayed as multiple cylinders.



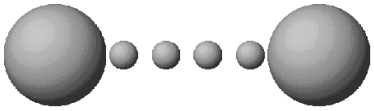
Triple covalent bonds

Triple covalent bonds share six electrons between two atoms, in three bonds created by the overlap of three orbitals on each atom. Each atom contributes three of its valence electrons to the bond. The following example shows a triple covalent bond displayed as multiple cylinders.



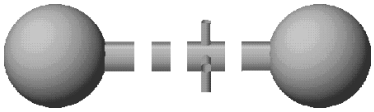
Weak bonds

Weak bonds allow you to explicitly represent the weak interactions between two atoms. A common example is the hydrogen bond, shown below in the multiple cylinders display style.



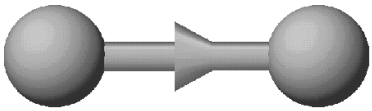
Ionic bonds

Ionic bonds represent strong attractions between centers of opposite charge. The electrons that participate in ionic bonds are localized at the negatively-charged atom. The following example shows an ionic bond in the multiple cylinders display style.



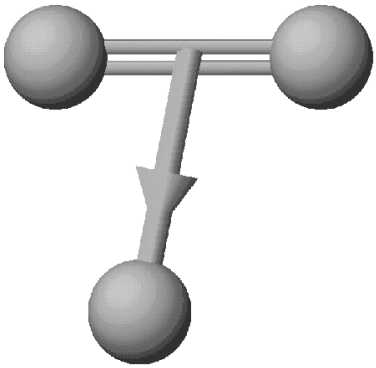
Coordinate covalent bonds

Coordinate covalent bonds or dative bonds are formed when a lone pair from one atom combines with an empty orbital of another atom. The following example shows a coordinate bond in the multiple cylinders display style.



π coordination bonds

These bonds involve donation of electrons from a π bond to an empty orbital of a metal. The only way to create π coordination bonds is to click and drag with the Atom/Bond tool away from the center of a bond to an empty location in the workspace, or from one existing atom to another. The following example shows a π coordination bond in the multiple cylinders display style.



6 Viewing Chemical Samples

Overview

This chapter describes how to use the CAChe workspace to:

- change the appearance of chemical samples, by viewing atoms and bonds in a number of different display options, without changing molecular structure
- customize display attributes for workspace objects, such as the color assigned to elements, the appearance of atom and bond properties, the appearance of workspace text and lines, and the perspective from which you view your chemical sample
- save customized workspace settings
- build crystal structures.

Contents

CAChe display options **6-2**
Using CAChe model types **6-4**
Changing the appearance of atoms **6-8**
Changing atom labeling 6-8
Changing atom shape 6-11
Changing atom color 6-14
Hiding and displaying electrons 6-16
Hiding atoms **6-18**
Hiding and displaying selected atoms 6-18
Hiding and displaying hydrogen atoms 6-19
Changing the appearance of bonds **6-21**
Changing bond shape 6-21
Changing bond color 6-25
Hiding bonds **6-28**
Hiding and displaying selected bonds 6-28
Viewing selection only **6-30**
Coloring by molecules **6-31**
Viewing multiple windows **6-32**
Viewing chemical sample data **6-33**
Selecting chemical sample data 6-34
Editing chemical sample data 6-35
Changing view settings **6-37**
Changing element color 6-37
Editing the color palette 6-38
Changing drawing settings 6-43
Changing workspace perspective and distance 6-44
Changing workspace stereo display 6-46
Changing view settings for valence 6-48
Saving settings **6-51**
Building crystal structures **6-54**
Selecting a space group 6-55
Defining cell parameters 6-57
Defining fractional coordinates 6-58
Building asymmetric atoms 6-60
Building a molecular crystal 6-60
Building an infinite lattice 6-62
Displaying and hiding crystal boundaries 6-63
Creating CrystalStructure files 6-63
ShelX files 6-65

CAChe display options

CAChe offers many different options for displaying atoms and bonds so that you can easily change the appearance of your entire chemical sample, or selected portions only, without changing the molecular structure.

This allows you to view different representations of your chemical sample at varying stages of your work. Choosing a new display style can help you visualize certain aspects or properties of your molecule more clearly.

CAChe offers the following display options for your chemical sample:

- shape, size, and shading options for atoms and bonds
- ability to show or hide atoms and bonds of a certain type
- ability to display electrons
- customizable color palette for workspace objects
- labeling options for atoms and bonds
- drawing settings for the display of text and lines in the workspace or in files containing graphs.



Refer to Chapter 19, *"Investigating Biomolecules"*, for additional information on viewing and displaying biomolecules.

While you can customize the display of your molecule by combining many different combinations of viewing options for atom and bond properties, CAChe also offers the following five built-in model styles available from the **View** menu:

- **Lines** - displays atoms as their atomic symbol, and bonds as multiple lines. Colors are not changed. The lines are not z-buffered, improving speed of rotation.
- **Lines Only** - displays atoms as small circles, and bonds as multiple small cylinders scaled to 0.04Å. Colors are not changed. The cylinders are z-buffered, improving depth perception for large molecules.

- **Cylinders** - displays atoms as small shaded spheres with a van der Waals radius of 1Å scaled to 0.05Å, and bonds as multiple cylinders scaled to 0.1Å. Colors are not changed.
- **Ball and Cylinder** - displays atoms as shaded spheres with a van der Waals radius of 1Å scaled to 0.2Å, and colored by element, and bonds as multiple cylinders scaled to 0.1Å, colored by atom color
- **Space Filling** (Corey-Pauling-Kolton model) - displays atoms as shaded spheres with a van der Waals radius of 1Å scaled to 1.0Å, and colored by element
- **Partial Charge and Calculated Bond Order** - displays atoms as shaded spheres with a partial charge of 1 a.u. scaled to 1.0Å, and colored by partial charge polarity (+/-), and bonds as single cylinders scaled to 0.1Å for a calculated bond order of 1, colored by calculated bond order.

The Partial Charge and Calculated Bond Order model style is enabled only if you have first run a partial charge or calculated bond order experiment on your chemical sample.



Refer to Chapter 16, *"Investigating Atom and Bond Properties"*, for information on running both a partial charge experiment and a calculated bond order experiment.

Using CAChe model types

To view your chemical sample as a line drawing

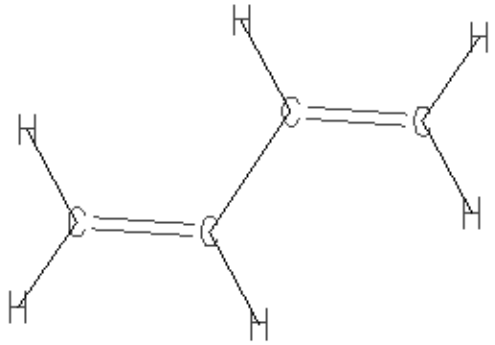
1. Select the portion of your molecule that you want displayed as a line drawing by clicking on objects with a selection tool.

   The objects are highlighted to show that they are selected.

2. Choose **View | Lines**.

   Atoms are displayed as their atomic symbol label, and bonds as multiple lines, colored by atom color. Atom colors are not changed. To color selected atoms by element, choose **View | Color by Element**.

   The following example shows a molecule displayed as a line drawing.



To view your chemical sample as a line only drawing

1. Select the portion of your molecule that you want displayed as a line only drawing by clicking on objects with a selection tool.

   The objects are highlighted to show that they are selected.

2. Choose **View | Lines Only**.

   Atoms are displayed as small circles, and bonds as multiple small z-buffered cylinders, colored by atom color. Atom colors are not changed. To color selected atoms by element, choose **View | Color by Element**.

To view your chemical sample as a ball and cylinder model

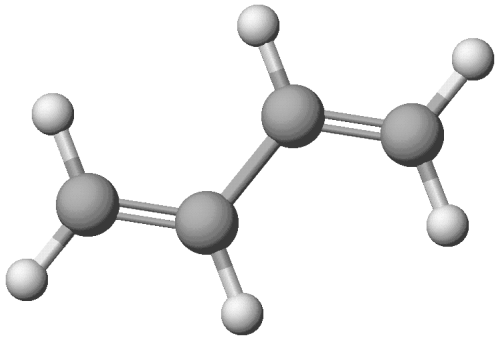
1. Select the portion of your molecule that you want displayed as a ball and cylinder model by clicking on objects with a selection tool.

   The objects are highlighted to show that they are selected.

2. Choose **View | Ball & Cylinder**.

   Atoms are displayed as shaded spheres with a van der Waals radius of 1Å scaled to 0.2Å.Bonds are displayed as multiple cylinders scaled to 0.1Å, colored by atom color. Atom colors are not changed. To color selected atoms by element, choose **View | Color by Element**.

   The following example shows a molecule displayed as a ball and cylinder model.



To view your chemical sample as a space filling (CPK) model

1. Select the portion of your molecule that you want displayed as a space filling model by clicking on objects with a selection tool.

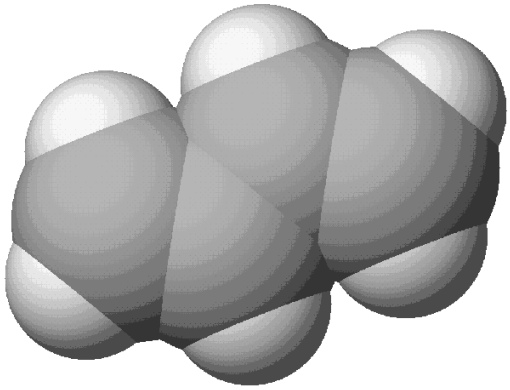
   The objects are highlighted to show that they are selected.

2. Choose **View | Space Filling**.

   Your molecule appears as a CPK (Corey-Pauling-Kolton) model with atoms displayed as shaded spheres with a van der Waals radius of 1Å scaled to 1.0Å. Bonds are displayed as single cylinders scaled to 0.000Å. Atom colors are not changed. To

color selected atoms by element, choose **View | Color by Element**.

The following example shows a molecule displayed as a space filling model.



To view your chemical sample by partial charge and calculated bond order

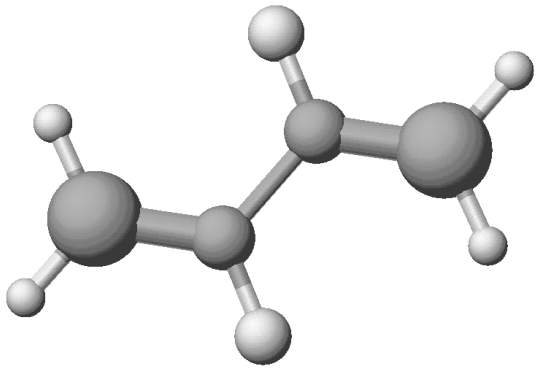
1. Run a partial charge experiment or a calculated bond order experiment on your chemical sample.
2. Select the portion of your molecule that you want displayed as by partial charge and calculated bond order by clicking on objects with a selection tool.

   The objects are highlighted to show that they are selected.
3. Choose **View | Partial Chg and Calc. Bond Order**.

Atoms are displayed as shaded spheres with a partial charge of 1 a.u. scaled to 1.0Å, and colored by partial charge polarity (+/-). Bonds are displayed as single cylinders scaled to 0.1Å for a calculated bond order of 1, colored by calculated bond order.

Refer to Chapter 16, *"Investigating Atom and Bond Properties"*, for information on running both a partial charge experiment and a calculated bond order experiment.

The following example shows a molecule displaying partial charge and calculated bond order.



Changing the appearance of atoms

Atoms can be represented by a variety of symbols that depict different kinds of information, such as spheres and space-filling spheres, or as combinations of symbols and spheres.

📖 NOTE The display style you choose to represent your chemical sample has no impact on its structure, or on any experiments you run using that chemical sample.

CAChe allows you to change the following aspects of an atom's appearance:

- atom labeling
- atom shape
- atom color
- the electrons of an atom.

Changing atom labeling

Choose from the following selection of atom labels:

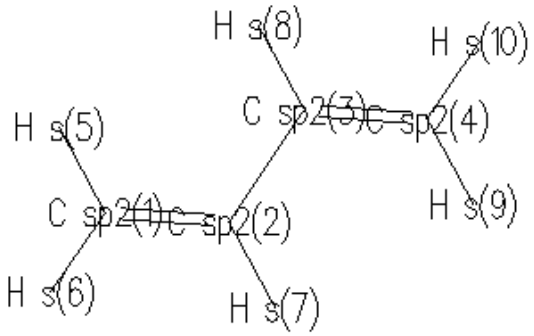
- atomic symbol - displays the atom symbol; e.g., **C** for carbon
- hybridization - displays the atom hybridization; e.g., **sp^3**
- charge - displays the atomic charge; e.g., **+1**
- partial charge - displays the calculated partial charge (as long as you have run a partial charge experiment on your chemical sample first)
- atom number - displays the CAChe atom number.

  CAChe assigns a unique number to each atom, and numbering is in the same order that you added the atoms to the workspace.

If you delete an atom from your chemical sample, the associated atom number is also deleted, creating a gap in the sequential order of atom numbers. The deleted atom's number is assigned to the next atom you add to the workspace.

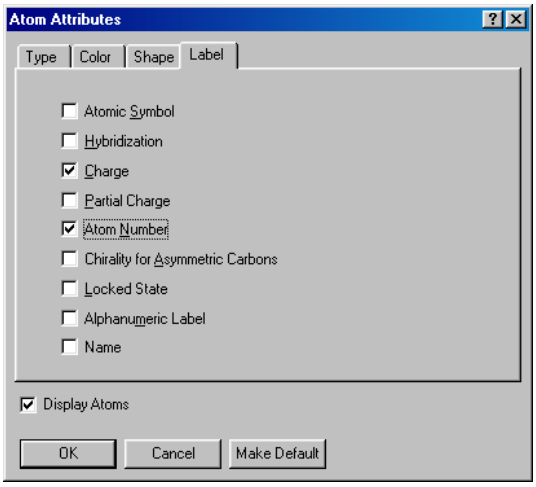
- chirality for asym. carbons - indicates which asymmetric carbon atoms are chiral centers; e.g., **R** or **S**
- locked state - indicates whether the atom is locked (**L**), and whether the lock is broken (**LB**).

  The following example shows a molecule's atoms displaying atom symbol, hybridization, and atom number labels.



To change atom labeling

1. Select the atoms for which you want to display labels by clicking on the atoms with a selection tool.
2. Choose **View** | **Atom Attributes** to display the Atom Attributes dialog box.



3. Select the **Label** tab to display the following list of labeling options for atoms:
   - atomic symbol
   - hybridization
   - charge
   - partial charge
   - atom number
   - chirality for asymmetric carbons
   - presence of locks on the atom
   - the alphanumeric label
   - name.

   If the chemical sample is from a PDB file, the **Name** is the PDB atom name.
4. Select the check box next to the display features you require for

each selected atom.

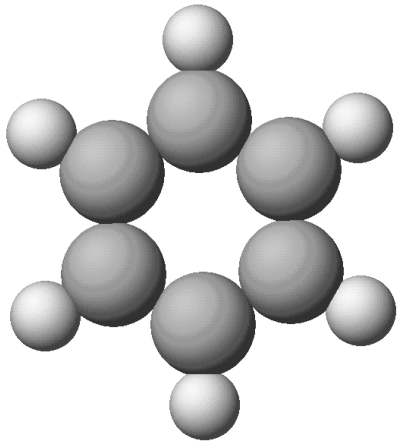
5. Select **OK** to close the Atom Attributes dialog box.

   The labels you chose are displayed against the atoms you selected.

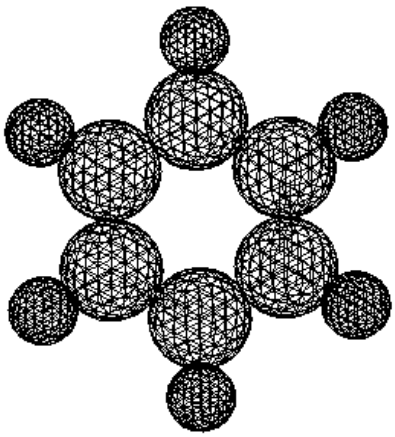
Changing atom shape

View atoms as three types of spheres:

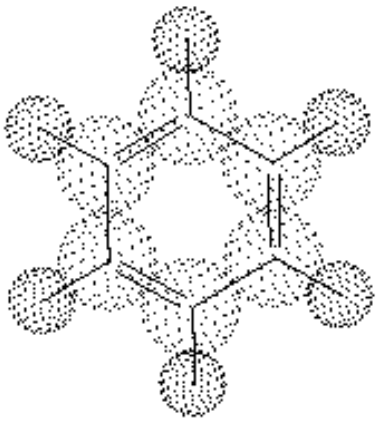
- shaded spheres - atoms are displayed as a shaded space-filling representation.



- wireframe spheres - atoms are displayed as a wireframe space-filling representation.



- dotted spheres - atoms are displayed as a dotted space-filling representation.



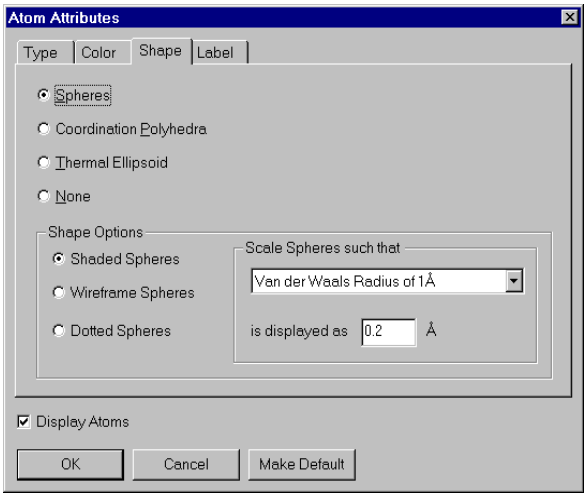
Change the radius of a sphere to represent:

- the van der Waal's radius
- the covalent radius
- a radius proportional to the calculated atomic partial charge property - only available if you have run a partial charge or calculated bond order experiment on your chemical sample.

Scale a sphere by specifying a radius size relative to 1Å.

To change atom shape

1. Select the atoms that you want to change shape by clicking on the atoms with a selection tool.
2. Choose **View** | **Atom Attributes** to display the Atom Attributes dialog box.



3. Select the **Shape** tab.
4. Choose one of the following options as the representation for the selected atoms:
   - **Spheres** radio button, proceed to step 5
   - **Coordination Polyhedra** radio button, proceed to step 8
   - **Thermal Ellipsoid** radio button, proceed to step 9
   - **None** radio button, to hide the selected atoms. Proceed to step 10.
5. From the following list in the **Shape Options** panel, select the shape option you want to apply to each selected atom:
   - **Shaded Spheres** radio button
   - **Wireframe Spheres** radio button
   - **Dotted Spheres** radio button.

6. Select the arrow button in the **Scale Spheres such that** box and choose a scaling option from the drop-down list.
7. Enter the factor by which you want to scale the radius in the **is displayed as** text box. Proceed to step 10.
8. Enter a value in the **Polyhedra Scale Factor** text box in the **Shape Options** panel. Proceed to step 10.

   The coordination polyhedra will be scaled by the factor you have entered.
9. Enter a value in the **Probability** text box in the **Shape Options** panel to determine the probability at which the ellipsoid is represented.
10. Select **OK** to apply the changes and to close the Atom Attributes dialog box.

    The selected atoms are displayed as the spheres you specified, with a radius representing the scaling options you chose.

Changing atom color

Color atoms by:

- element - colors the selected atoms with the element color from the periodic table settings.
- partial charge polarity - colors the selected atoms by the calculated partial charge polarity. Atoms with a positive partial charge are colored with color index 2 (usually red). Atoms with a negative partial charge are colored with color index 3 (usually yellow). An experiment which produces partial charge must have been run on your chemical sample before this choice produces useful results.
- specific color - colors the selected atoms with a specific color that you choose from a drop-down list displaying 12 colors.



Refer to *"Changing view settings"*, p 6-37, for information on how to edit element color settings for the periodic table.

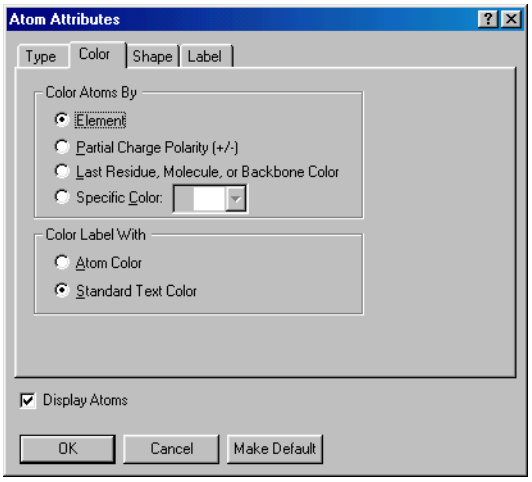
Use the following options to change the color of atom labels:

- atom color - colors labels on the selected atoms with the same color selected in the **Color atoms by** panel of the **Color** tab options.
- standard text color - colors labels on the selected atoms with the standard text color.

Refer to *"Editing the color palette"*, p 6-38, for information on changing the standard text color by editing the CAChe color palette.

To change atom color and atom label color

1. Select the atoms that you want to change color by clicking on the atoms with a selection tool.
2. Choose **View** | **Atom Attributes** to display the Atom Attributes dialog box.



3. Select the **Color** tab to display the following list of color options for atoms:
   - color atoms by element
   - color atoms by partial charge polarity
   - by last residue, molecule or backbone color
   - color atoms by specific color.
4. In the **Color Atoms By** panel, select the radio button next to the color option you want to apply to each selected atom, ensuring

Using

that the relevant radio button is enabled.

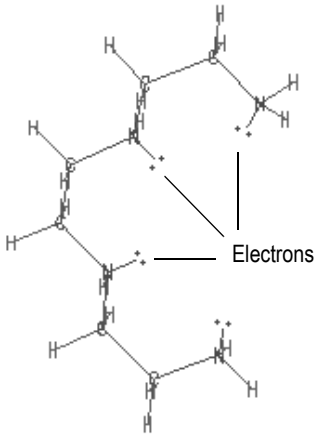
5. If you select the **Specific Color** radio button, also select the arrow button in the box and choose a color from the drop-down list.
6. In the **Color Label With** panel, select the radio button next to the color option you want to apply to the label of each selected atom, ensuring that the relevant radio button is enabled.
7. Select **OK** to close the Atom Attributes dialog box.

   The selected atoms and their atom labels are displayed in the colors you chose.

Hiding and displaying electrons

CAChe can add representations of non-bonded valence electrons to your chemical sample. You can display or hide electrons in the chemical sample. When you hide electrons, they remain part of the chemical sample. Hiding electrons has no effect on calculations run on the chemical sample during an experiment.

The following example shows electrons displayed in the workspace.



To display electrons

1. When electrons are hidden, choose **View** | **Show Electrons**.

   A check mark is displayed next to the drop-down list option to indicate that electrons are visible. All of the electrons in the

workspace are displayed.

To hide electrons

1. When electrons are visible, choose **View | Show Electrons**.

   The check mark next to the drop-down list option disappears to indicate that electrons are hidden. All of the electrons in the workspace are hidden.

Hiding atoms

You may want to view part or all of your chemical sample, without displaying its atoms, so that you can view other aspects of your molecule more clearly. Hiding atoms simplifies the appearance of your chemical sample, and increases the speed of manipulating the molecule around the workspace.

CAChe allows you to:

- hide and display selected atoms in your sample
- hide and display all of the hydrogen atoms in your sample.

Hiding and displaying selected atoms

When you hide selected atoms, the atoms are hidden in the workspace but remain part of your chemical sample. Hiding atoms does not affect any experiments you subsequently run on the chemical sample.

To hide selected atoms

1. Select the atoms that you want to hide by clicking on them with a selection tool.
2. Do one of the following:
   - Choose **View | Hide Selected**.
   - or,
   - Choose **View | Atom Attributes** to display the Atom Attributes dialog box. Select the **Display Atoms** check box so that it is not checked. (The **Display Atoms** check box is displayed no matter which tab is currently selected in the Atom Attributes dialog box.) Select **OK** to close the Atom Attributes dialog box.

   The selected atoms are hidden and then the visible objects are selected.

To hide unselected atoms

1. Select the atoms that you want to remain visible by clicking on them with a selection tool.
2. Choose **View | Hide Unselected**.

   The atoms that are not selected are hidden.

   You will find this command very useful when working with complex molecules because it allows you to see clearly selected objects by quickly hiding all those that are not selected.

To display hidden selected atoms

Do one of the following:

1. Choose **View | Show All**,

   or

1. Do one of the following to select all atoms:
   - Choose **Edit | Select All**.
   - Press **Ctrl A**.
2. Choose **View | Atom Attributes** to display the Atom Attributes dialog box.
3. Select the **Display Atoms** check box so that it is enabled.

   A check mark appears in the **Display Atoms** check box.
4. Select **OK** to close the Atom Attributes dialog box.

   All of the atoms in the workspace are now visible.

Hiding and displaying hydrogen atoms

You can show or hide all the hydrogen atoms in your chemical sample, without deleting the atoms. As with hiding atoms, hiding hydrogen atoms does not affect any calculations you run on the chemical sample while hydrogens are hidden.

To hide hydrogen atoms

1. When hydrogens are visible, choose **View | Suppress Hydrogens**.

A check mark is displayed next to the drop-down list option to indicate that hydrogens are hidden. Depending upon the setting in **Options | Valence Settings**, either all the hydrogen atoms in the workspace are hidden or only the hydrogen atoms connected to carbon are hidden.

To display hydrogen atoms

1. When hydrogens are hidden, choose **View | Suppress Hydrogens**.

   The check mark that is displayed next to the drop-down list option disappears to indicate that hydrogens are visible. All the hydrogen atoms in the workspace are visible.

Exceptions to hiding hydrogen atoms

You cannot hide hydrogen atoms that are attached to a locked atom, or hide locked hydrogen atoms.

Refer to Chapter 8, *"Investigating Molecular Geometry"*, for details about locked atoms.

You also cannot hide hydrogen atoms that are attached to an atom that has not had its valence checked by choosing **Beautify | Valence** or **Beautify | Comprehensive**.

Refer to Chapter 5, *"Modifying Chemical Samples"*, for details about the **Beautify** menu options.

You can also choose to keep hydrogens displayed if they are attached to atoms with valence exceptions by choosing **Options | Valence Settings**. You can also choose to keep hydrogens displayed if they are attached to atoms other than carbon by choosing **Options | Valence Settings**.

Refer to *"Changing view settings for valence"*, p 6-48, for details about the **Options | Valence Settings** menu option.

Changing the appearance of bonds

CAChe allows you to change the shape and color of a bond's appearance. As with changing the appearance of atoms, choosing another display style for bonds has no impact on a chemical sample's structure, or on any experiments you run using that chemical sample.

Changing bond shape

Bonds can be represented as:

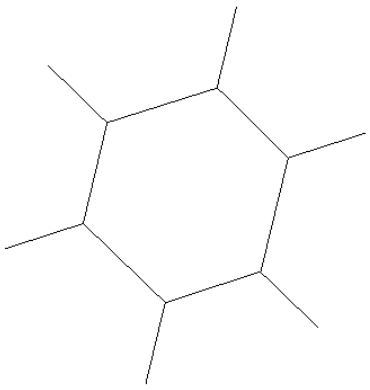
- single lines
- multiple lines
- single cylinders
- multiple cylinders.

Scale the radius of a cylinder by:

- specifying a relative size in angstroms for each cylinder
- specifying a relative size in angstroms for a formal bond order of 1
- specifying a relative size in angstroms for a calculated bond order of 1. This option is only useful after a calculated bond order experiment has been run on your chemical sample.

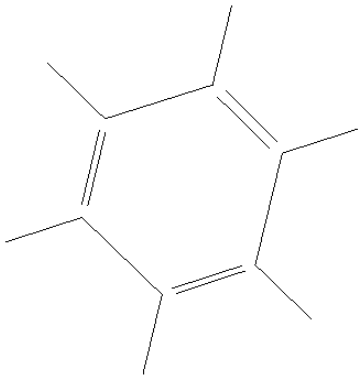
Single lines

All bond types are displayed as a single line with one line connecting the two atoms, as shown in the following example.



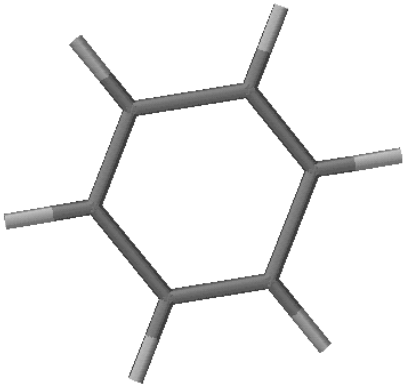
Multiple lines

Bonds are displayed as lines, with the number of lines connecting the two atoms corresponding to the bond type. For example, a double bond is displayed as two lines, as shown in the following example.



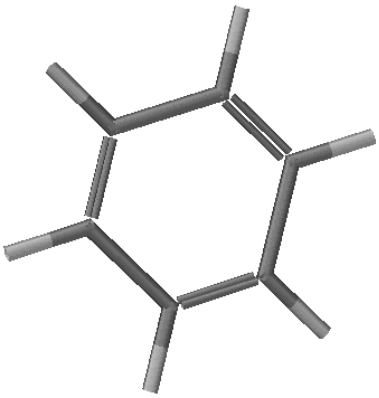
Single cylinders

All bond types are displayed as a single cylinder with one cylinder connecting the two atoms, as shown in the following example.



Multiple cylinders

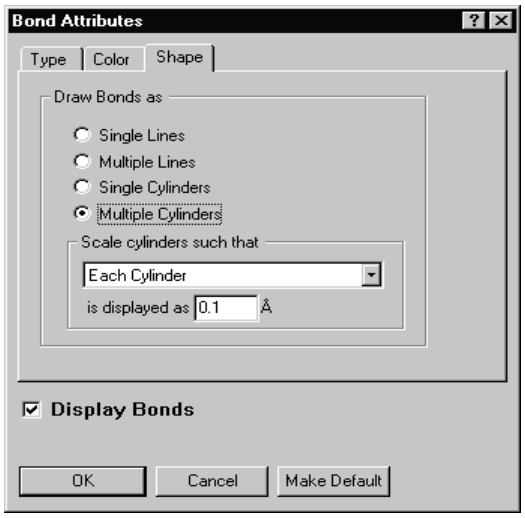
Bonds are displayed as cylinders, with the number of cylinders connecting the two atoms corresponding to the bond type. For example, a double bond is displayed as two cylinders, as shown in the following example.



To change bond shape

1. Select the bonds that you want to change shape by clicking on the bonds with a selection tool.

2. Choose **View** | **Bond Attributes** to display the Bond Attributes dialog box.



3. Select the **Shape** tab to display the following list of shape options for bonds:
   - single lines
   - multiple lines
   - single cylinders
   - multiple cylinders.
4. In the **Draw bonds as** panel, select the radio button next to the shape option you want to apply to each selected bond, so that the relevant radio button is enabled.
5. Select the arrow button in the **Scale cylinders such that** box and choose a scaling option from the drop-down list.
6. Click in the **is displayed as** text box and enter the factor by which you want to scale the radius of each selected bond.
7. Select **OK** to close the Bond Attributes dialog box.

   The selected bonds are displayed in the shape you specified, with a radius representing the scaling options you chose.

Changing bond color

Bonds can be colored by:

- atom color - colors the selected bonds with the same color specified for the atom attached at each end of the bond. Atom color is specified using the Atom Attributes dialog box.



Refer to *"Changing the appearance of atoms"*, p 6-8, for more information on specifying atom color.

For example, if a bond is drawn between an atom colored by a specific color blue and a carbon atom colored by element type, the bond will be half blue and half black.

- atom element color - colors the selected bonds with the element color from the periodic table settings.



Refer to *"Changing view settings"*, p 6-37, for information on how to edit element color settings for the periodic table.

- bond type - colors the selected bonds by the type of bond. Single bonds are colored with color index 3, double bonds are colored with color index 4, triple bonds are colored with color index 8, weak bonds are colored with color index 5, coordinate bonds are colored with color index 7, and ionic bonds are colored with color index 1.



Refer to *"Editing the color palette"*, p 6-38, for information on changing the assigned bond type colors by editing the CAChe color palette.

- calculated bond strain - colors the selected bonds by the calculated bond strain. The calculated bond strain is mapped onto the bond order values, and the color indexes used are the same as for bond type.

  This option is only useful after a calculated bond strain experiment has been run on your chemical sample.

- calculated bond order - colors the selected bonds by the calculated bond order. Bond order values are rounded to the nearest integer, and the color indexes used are the same as for bond type.

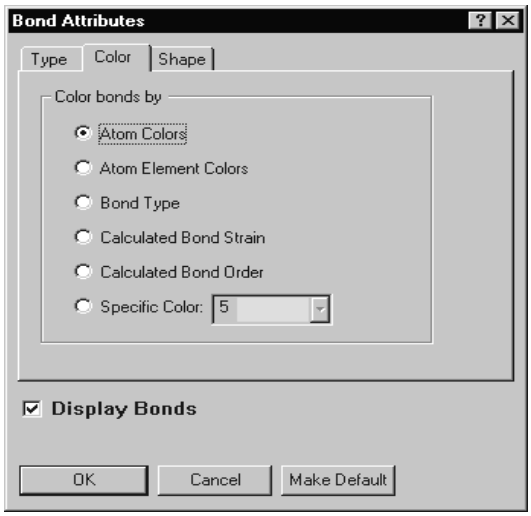
  This option is only useful after a calculated bond order experiment has been run on your chemical sample.

- specific color - colors the selected bonds with a specific color that you choose from a drop-down list displaying 12 colors.

Refer to *"Editing the color palette"*, p 6-38, for information on changing the colors displayed in the drop-down list by editing the CAChe color palette.

To change bond color

1. Select the bonds that you want to change color by clicking on them with a selection tool.
2. Choose **View** | **Bond Attributes** to display the Bond Attributes dialog box.



3. Select the **Color** tab to display the following list of color options for bonds:
   - color bonds by atom colors
   - color bonds by atom element colors
   - color bonds by bond type
   - color bonds by calculated bond strain
   - color bonds by calculated bond order
   - color bonds by specific color.
4. Select the radio button next to the coloring option you want to apply to each selected bond, so that the relevant radio button is enabled.
5. To assign a specific color to selected bonds, select the arrow button in the **Specific Color** box and choose a color from the drop-down list.
6. Select **OK** to close the Bond Attributes dialog box.

   The selected bonds are displayed in the colors you chose.

Hiding bonds

CAChe allows you to:

- hide and display selected bonds in your sample.

You can hide the bonds in your chemical sample in exactly the same way that you can hide atoms. The bonds are hidden from view in the workspace, but are still present in your molecule. Hiding bonds does not affect any experiments you run on your chemical sample while bonds are hidden.

Hiding and displaying selected bonds

To hide selected bonds

1. Select the bonds that you want to hide by clicking on them with a selection tool.

   Then do one of the following:

2. Choose **View | Hide Selected**

   The selected bonds are not visible in the workspace.

Alternatively,

1. Select the bonds that you want to hide by clicking on them with a selection tool.
2. Choose **View | Bond Attributes** to display the Bond Attributes dialog box.
3. Select the **Display Bonds** check box so that it is disabled.

   The **Display Bonds** check box is displayed no matter which tab is currently selected in the Bond Attributes dialog box.
4. Select **OK** to close the Bond Attributes dialog box.

   The selected bonds are not visible in the workspace.

To display hidden bonds

Do one of the following:

1. Choose **View | Show All**,

   All of the bonds in the workspace are now visible.

Alternatively,

1. Do one of the following to select all the objects in the workspace:
   - Click on an empty area of the workspace with a selection tool.
   - Choose **Edit | Select All**
   - Press **Ctrl A**.
2. Choose **View | Bond Attributes** to display the Bond Attributes dialog box.
3. Select the **Display Bonds** check box so that it is enabled.

   A check mark appears in the **Display Bonds** check box.
4. Select **OK** to close the Bond Attributes dialog box.

   All of the bonds in the workspace are now visible.

Viewing selection only

Simplifying the view of giant molecules, crystal lattices and complex chemical samples often aids understanding and analysis. You can simplify a view by displaying only selected objects like backbone atoms.

To show only the selection

1. From the 3D Structure window or Sample Property View, choose **View | Show Selection Only**.

   All displayable objects such as atoms, bonds, and labels which are selected are displayed and all other objects are hidden. The menu item **View | Show Selection Only** is checked indicating that objects are hidden.

To display hidden objects

1. From the 3D Structure window or the Sample Property View, choose to **View | Show Selection Only** uncheck it and restore the display of all objects.

TIP When you are viewing selections only, the visible objects change when you change selection. Viewing selection only is often used with either a Sample Property view or the Sequence View Window and selections are made in one of those windows.

Often a better way to simplify the view, is to hide atoms and bonds with the **View | Hide Unselected** and **View | Hide Selected** commands.

Coloring by molecules

Giant molecules, crystal lattices and complex chemical samples often contain many separate molecules or chains. You can visually separate molecules by coloring each with a different color.

To color molecule

1. From the workspace, choose **View | Color by Molecule**.

   All molecules that contain more than three atoms and have at least one atom selected are identified and each is colored in turn with a color from the twelve CAChe atom colors. Unless the colors have been changed with **View | Color Palette**, the colors used are cyan, dark red, gold, green, blue, white, grey, red yellow, bright green, dark blue, purple. If there are more than twelve molecules present, the colors are reused.

Viewing multiple windows

You can open many 3D structure windows and one sample properties window for each chemical sample. When you open a new 3D structure window of the same chemical sample file, CAChe displays the molecular structure at a different orientation. Opening multiple document windows allows you to look at your chemical sample from a number of different perspectives, or in different ways, simultaneously.

If you change the chemical structure in one window, all other windows containing the same chemical sample reflect those changes.

To open a new 3D structure window of a chemical sample

1. Choose **Window** | **New 3D Structure Window**.

   A new window opens, displaying the contents of the active document window at a different perspective.

To open a new sample properties window of a chemical sample

1. Choose **Analyze** | **Chemical Properties Spreadsheet**.

   A new window opens, displaying the contents of the active document window as a spreadsheet workbook.

Viewing chemical sample data

The CAChe chemical sample is a database of information about your chemical sample. You can view and modify the information in a sample property workbook.

To open a new window showing chemical sample properties

1. Choose **Analyze** | **Chemical Properties Spreadsheet**.

   A new window opens, displaying the contents of the active document chemical sample in a workbook.

ChemicalSample2:2*

	A Atom List	B ID	C Formal Charge	D X Coordinate (angstrom)	E Y Coordinate (angstrom)	F Z Coordinate (angstrom)	G Partial Charge	H Name	I Temperature Factor	J Atom Position	K Hybridization
1	N1	1	0	16.864	14.059	3.442	0.000	N	6.220	BB	sp3
2	C2	2	0	16.868	12.814	4.233	0.000	CA	4.450	BB	sp3
3	C3	3	0	15.583	12.775	4.990	0.000	C	4.390	BB	sp2
4	O4	4	0	15.112	13.824	5.431	0.000	O	7.040	0	sp
5	C5	5	0	18.060	12.807	5.200	0.000	CB	5.420	0	sp3
6	O6	6	0	19.233	12.892	4.380	0.000	OG1	7.870	0	sp
7	C7	7	0	18.117	11.578	6.092	0.000	CG2	6.880	0	sp3
8	H8	8	0	16.007	14.241	3.093	0.000	1H	6.170	0	s
9	H9	9	0	17.087	14.800	3.997	0.000	2H	5.690	0	s
10	H10	10	0	17.481	14.013	2.750	0.000	3H	5.690	0	s
11	H11	11	0	16.940	12.048	3.605	0.000	HA	4.300	0	s
12	H12	12	0	18.008	13.641	5.765	0.000	HB	5.820	0	s
13	H13	13	0	19.761	13.553	4.647	0.000	HG1	6.620	0	s
14	H14	14	0	17.940	10.768	5.540	0.000	1HG2	6.360	0	s
15	H15	15	0	18.983	11.488	6.531	0.000	2HG2	6.130	0	s

Atoms | Bonds | Groups | Notes | Orbitals

In the chemical sample, atoms and their properties appear in the **Atoms** worksheet, bonds in the **Bonds** worksheet, and residues in the **Groups** worksheet. The **Orbitals** worksheet keeps track of nonbonded electron pairs so that the valence can be checked. The **Calculations** worksheet tracks the sequence of modeling calculations that have been performed.

The sample properties window is a workbook view of your chemical sample. As you work with the chemical sample using either the 3D Structure workspace or the Chemical Properties workbook, you add or change chemical sample information. The changes are immediately updated in the 3D Structure windows and Chemical Properties workbook (sample properties window). Save the workspace as a chemical sample file (`.csf`) to preserve all of the information you have added. If you save chemical samples in other formats, information such as rendering style, and computed atom properties will be lost.

Selecting chemical sample data

You can select objects in the chemical sample file such as atoms, bonds, labels, and groups directly from a spreadsheet in the workbook. Selection from a worksheet is often the easiest way to choose specific atoms, bonds, groups, labels or other objects.

To select all chemical sample objects

1. In the Chemical Properties Spreadsheet, choose **Edit | Select All**.

   All objects in the chemical sample on all worksheets are selected and displayed as greyed. Objects displayed in any workspaces of the same chemical sample are highlighted.

To select a chemical sample object

1. In the Chemical Properties workbook, choose the tab for the kind of object, e.g. Atoms or Bonds.
2. Click on the row number. The row number is contained in the first column of the spreadsheet.

   The row background is greyed, all other objects are deselected and the object is selected. The same object displayed in any workspaces of the same chemical sample are highlighted.

To toggle the selection of a chemical sample object

1. In the Chemical Properties workbook, choose the tab for the kind

of object, e.g. **Atoms** or **Bonds**.

2. While holding the **Ctrl** key, click on the row number. The row number is contained in the first column of the spreadsheet.

   The selection state of the object is inverted and its display in any workspaces of the same chemical sample are updated. The selection of other objects is unchanged.

To extend the selection of chemical sample objects

1. In the Chemical Properties workbook, choose the tab for the kind of object that is currently selected, e.g. **Atoms** or **Bonds**.
2. While holding the **Shift** key, click on the row number.

   The row background is greyed from the first selected object to the current row, all other objects are deselected and the greyed objects are selected. Selected objects displayed in any workspaces of the same chemical sample are highlighted.

Editing chemical sample data

You can enter specific data into the chemical sample file such as precise atom coordinates or experimental UV/visible absorption spectra.

TIP Editing the value of atom IDs renumbers atoms in a molecule.

To enter chemical sample properties

1. In the Chemical Properties workbook, choose **Edit** | **Edit Property Values**.

   Editing of cells is enabled.

2. Click in a cell and type the new value.

   When you click out of the cell, the value is updated and all open workspace and sequence views are also immediately updated.

NOTE Editing the value of geometry labels does not alter the geometry.

To copy, cut, paste, and delete chemical sample properties

1. In the Chemical Properties workbook, choose **Edit | Edit Property Values**.

   Editing of cells is enabled.

2. Select a cell or information in a cell.
3. Choose one
   - **Edit | Copy**
   - **Edit | Cut**
   - **Edit | Paste**
   - **Edit | Delete**.

   The chosen operation is performed on the selection. Entire rows are selected by clicking on the row number.

Note that you can copy and paste between sample property worksheets, between chemical samples and to and from external applications like word processors and spreadsheets.

Changing view settings

CAChe allows you to customize display attributes for workspace objects, such as:

- the color assigned to elements
- the color assigned to atom and bond properties, workspace labeling, and text and background color
- text and line width for general workspace labeling
- the perspective from which you view your chemical sample.

You can also specify display criteria for showing and hiding hydrogen atoms and electrons in the workspace.

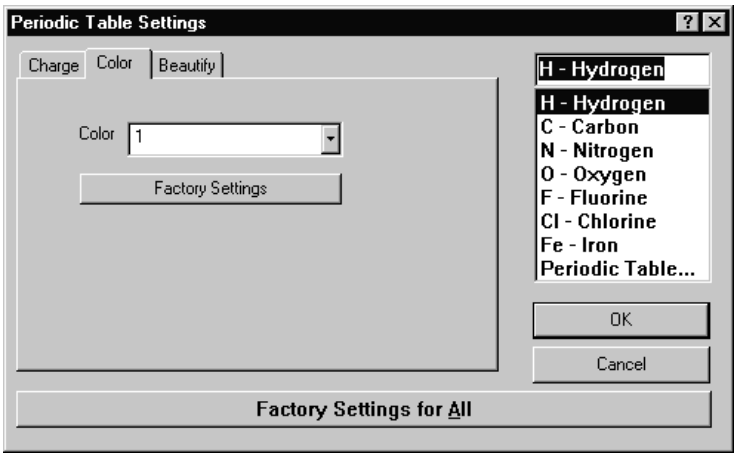
Changing element color

You can change the color assigned to any element in CAChe by editing the settings of the periodic table. Changes you make this way apply to all chemical sample files, not just the active document in the workspace.

To change element color

1. Choose **Options | Periodic Table Settings.**

   The Periodic Table Settings dialog box is displayed.



2. Do one of the following to select an element whose color you want to change:
   - Select an element in the Periodic Table Settings element list.
   - Double-click on **Periodic Table** to display the Periodic Table dialog box, and select an element by clicking on it and selecting **OK** to close the Periodic Table dialog box.
3. Select the **Color** tab to display the **Color** box.
4. Select the arrow button in the **Color** box and choose a color from the drop-down list of 12 colors.
5. Select **OK** to close the Periodic Table Settings dialog box.

   The new element color is applied to objects of the element type you chose from the drop-down list. Color changes apply to all saved chemical sample files, and all new objects of that element type drawn in the workspace.

📖 NOTE Select **Factory Settings** to restore default settings for element color for the element currently chosen in the Periodic Table Settings dialog box. **Factory Settings** is displayed when you select the **Color** tab.
Select **Factory Settings for All** to restore default settings to all elements for all options selected in the Periodic Table Settings dialog box.

You can also use the Periodic Table Settings dialog box to specify how an atom of a particular element type is corrected using the **Beautify** menu, and how the atom's radius is displayed for a particular atomic charge.

Refer to *"Defining valence rules"*, p 4-10 for more information on the Periodic Table Settings dialog box.

Editing the color palette

Change the color assigned to workspace objects, and atom and bond properties, by editing the CAChe color palette. The color palette matches one of 14 colors to a property or an object.

You can change any one of the fourteen colors by:

- choosing another pre-defined color
- creating a new custom color by specifying red, green, and blue color values, and hue, saturation, and luminosity values.

Out of the 14 colors in the palette, the first 12 colors are assigned an index number. These twelve colors appear in dialog boxes that allow you to choose a color for selected bonds and atoms, or for elements.

The remaining two colors in the color palette are not numbered, and allow you to change the workspace text color and background color.

You can change the color for the following atom and bond properties using the color palette:

- single bonds
- double bonds
- triple bonds
- ionic bonds
- weak bonds
- surface labels
- atom distance geometry labels
- bond angle geometry labels
- dihedral angle geometry labels
- improper torsion geometry labels.

You can change the color of the following workspace properties using the color palette:

- standard text color
- workspace background color.

When you edit the color palette, all the objects represented by that color will change to the new color.

For example, the color assigned to the index number 8 represents triple bonds and improper torsion geometry labels, and may

represent some elements, and parts of a calculated 3D surface generated by experiments.

When you edit this color, all objects represented by this color will change in the active workspace.

Refer to *"Changing the appearance of atoms"*, p 6-8, and *"Changing the appearance of bonds"*, p 6-21, for details about changing the color of selected atoms or bonds.

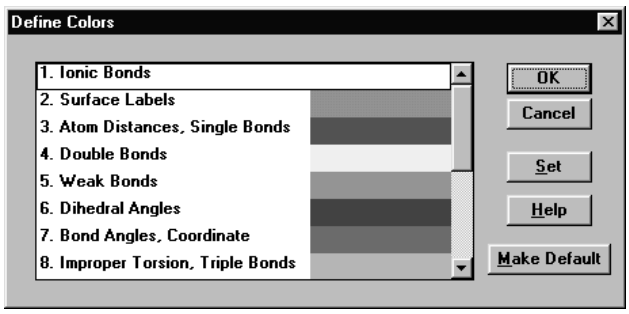
Refer to *"Changing element color"*, p 6-37, for details about changing the color of particular elements without affecting other objects that share the same color.

Viewing the color palette

To view the color palette

1. Choose **View** | **Color Palette**.

   The Define Colors dialog box is displayed. A scrolling list displays a color index number and associated properties and objects which are represented by the corresponding color.



2. Click and drag the scroll bar to view all 14 colors in the color palette.

Changing the color palette

When you change a color in the color palette, you can either:

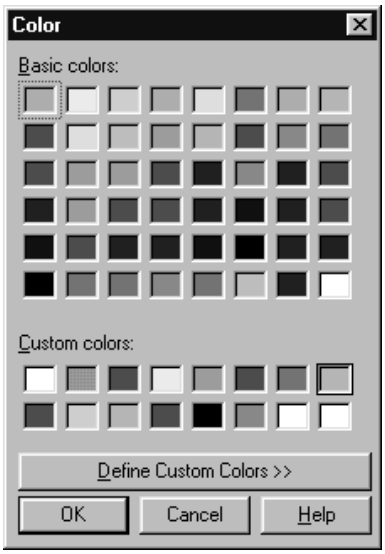
- choose a pre-defined color from a selection of basic Windows colors or custom colors
- create a new color from any of 16.8 million colors by adjusting red, green, and blue values, and hue, saturation, and luminosity values.

To change a color to a pre-defined color

1. Select the color you want to change by clicking on it in the Define Color dialog box scrolling list.

   A box is displayed around the list option to show that it is selected.

2. Select **Set** to display the Color dialog box.



3. Do one of the following:
   - Select one of the 48 basic Windows colors by clicking on a color box in the **Basic colors** panel.
   - Select a custom color by clicking on a color box in the **Custom colors** panel.

4. Select **OK** to close the Color dialog box.

   The new color replaces the color you selected in the Define Colors dialog box scrolling list.

5. Select **OK** to close the Define Colors dialog box.

   All workspace objects represented by that color index number are displayed in the new color.

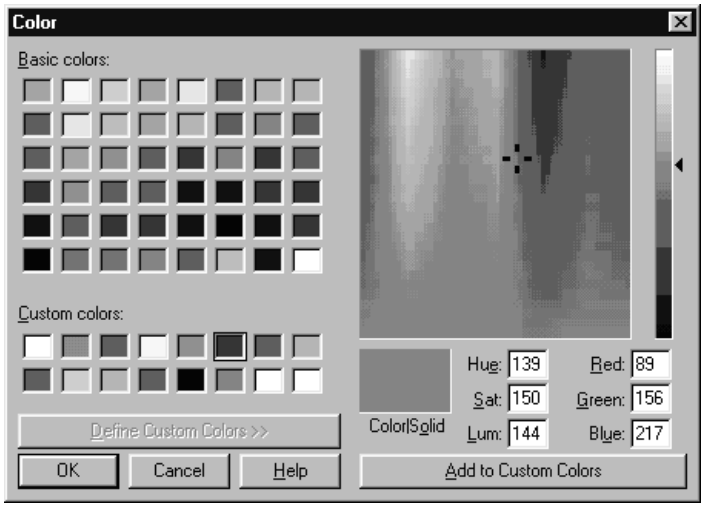
To change a color to a new custom color

1. Select the color you want to change by clicking on it in the Define Color dialog box scrolling list.

   A box is displayed around the list option to show that it is selected.

2. Select **Set** to display the Color dialog box.

3. Select **Define Custom Colors** to display a color picker square in an extended Color dialog box.



4. Do one of the following:

   Click and drag the crosshairs around the color picker square to choose a new color. Click and drag the slider at the right of the color picker square to adjust the luminosity value. The values in the **Red**, **Green**, and **Blue** text boxes, and the **Hue** and **Sat** text boxes, change as you drag the crosshairs around the square. The

value in the **Lum** text box changes as you drag the slider up or down.

- Click in the **Red**, **Green**, and **Blue** text box and enter the values you require for the new color. The values in the **Hue**, **Sat**, and **Lum** text boxes change accordingly. Click in the **Hue**, **Sat**, and **Lum** text boxes to change these values. The values in the **Red**, **Green**, and **Blue** text boxes change accordingly.

A sample of the color you are creating is displayed in the **Color|Solid** box.

5. Click on **Add to Custom Colors** when the color displayed in the **Color|Solid** box is the color you require.

   The new color appears in the **Custom colors** panel of the Color dialog box.

6. Select **OK** to close the Color dialog box.

   The new custom color replaces the color you selected in the Define Colors dialog box scrolling list.

7. Select **OK** to close the Define Colors dialog box.

   All workspace objects represented by that color index number are displayed in the new custom color.

Changing drawing settings

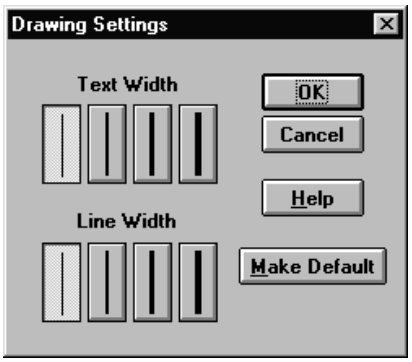
CAChe allows you to change the width of lines or text in the workspace. Workspace objects affected by changing drawing settings include geometry and search labels, atom labels, graph labels and axes.

The thinnest line width will give the fastest screen rendering, but prints as hair lines on high-resolution hard copy. Choose one of the other three line widths for lines that scale proportionately on the printer.

To change drawing settings

1. Choose **Options** | **Drawing Settings**.

   The Drawing Settings dialog box is displayed.



2. Select a text width by clicking on the button that displays the width you require.

   The currently active text width button is depressed to show that it is enabled.

3. Select a line width by clicking on the button that displays the width you require.

   The currently active line width button is depressed to show that it is enabled.

4. Select **OK** to close the Drawing Settings dialog box.

   Text and lines in the active workspace are displayed in the width you chose.

Changing workspace perspective and distance

You can change the perspective in which you view your chemical sample by aligning the view with an axis or plane in your molecular structure. You can also edit the viewing distance, and front and back clipping depths.

Align your workspace view with the following:

- x axis - enables you to view your chemical sample looking down the chemical sample's x axis
- y axis - enables you to view your chemical sample looking down the chemical sample's y axis
- z axis - enables you to view your chemical sample looking down the chemical sample's z axis.

- through selected atoms - enables you to view your chemical sample looking down the axis formed by two selected atoms or normal to the plane formed by three selected atoms. You must have either two or three atoms selected when you choose the View Settings command in order to use this option.

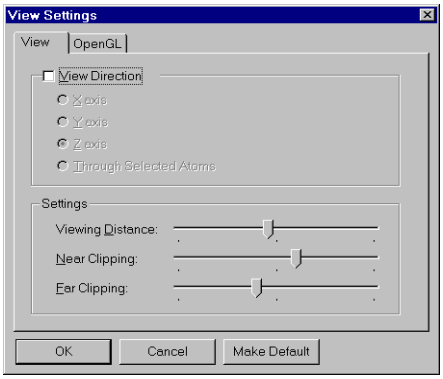
Alter viewing distance and depth using the following options:

- viewing distance - controls the perspective of images on the screen. Perspective can be exaggerated to enhance the 3D effect.
- near clipping - clips the front portions of your molecule as it encounters the front of the three-dimensional viewing box. This gives you a cross sectional view of the remaining portion of your molecule.
- far clipping - clips the back portions of your molecule as it encounters the back of the three-dimensional viewing box. This gives you a cross sectional view of the remaining portion of your molecule.

To change workspace perspective and distance

1. Choose **Options | View Settings.**

   The View Settings dialog box is displayed.



2. To align your workspace view with the x, y, or z axis, select the radio button next to the axis you require, so that the radio button is enabled.

3. To align your workspace view through selected atoms, select two or three atoms by clicking on them with a selection tool cursor.

   The **Through Selected Atoms** radio button is no longer grayed out.

4. Select the **Through Selected Atoms** radio button so that it is enabled.
5. To decrease the viewing distance of your molecule, click and drag the **Viewing Distance** slider to the left.
6. To increase the viewing distance of your molecule, click and drag the **Viewing Distance** slider to the right.
7. To shrink the front of the three-dimensional viewing box to clip your molecule, click and drag the **Near Clipping** slider to the left.
8. To expand the front of the three-dimensional viewing box to clip your molecule, click and drag the **Near Clipping** slider to the right.
9. To shrink the back of the three-dimensional viewing box to clip your molecule, click and drag the **Far Clipping** slider to the left.
10. To expand the back of the three-dimensional viewing box to clip your molecule, click and drag the **Far Clipping** slider to the right.

Changing workspace stereo display

If you have a Stereo license, you can improve the way in which your chemical sample is displayed in the workspace by using the following options:

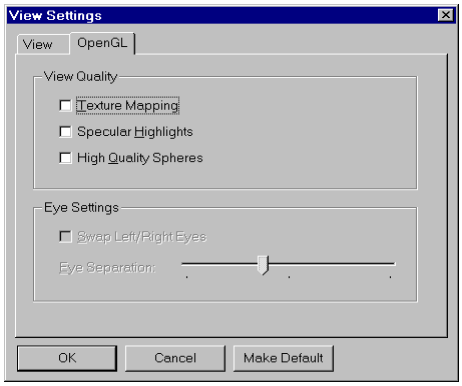
- texture mapping - enables you to improve the texture quality of your sample
- specular highlights - enables you to add specular highlights to the atoms in your sample
- high quality spheres - enables you to improve the precision of the atoms in your sample.

You can alter the eye settings, while wearing the stereo glasses, using the following option:

- eye separation - controls the stereo disparity, so that as you rotate the trackball, objects seem not to stretch as they rotate.

To change stereo display in the workspace

1. Choose **Options | View Settings.**
2. Select the **OpenGL** tab to display the following dialog box.



3. Select the required features from the following list of options in the **View Quality** panel:
   - **Texture Mapping**
   - **Spectral Highlights**
   - **High Quality Spheres**.

   Texture Mapping and Spectral Highlights cannot be chosen together. High Quality Spheres can be chosen with either option.
4. In the **Eye Settings** panel, select **Swap Left/Right Eyes** to correctly view the workspace while wearing the stereo glasses.
5. To adjust the stereoscopic view for your eyes, do one of the following:
   - click and drag the **Eye Separation** slider to the right to make objects appear deeper
   - click and drag the **Eye Separation** slider to the left to make objects appear flatter.

The stereo view in the workspace changes when you release the mouse button so that you can find the best separation for your eyes.

6. Select **OK** to close the View Settings dialog box.

Changing view settings for valence

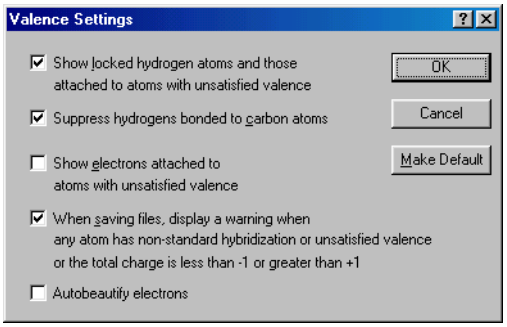
You can choose to keep hydrogens and electrons displayed if they are attached to atoms with valence exceptions. You can also choose to keep locked hydrogen atoms displayed. When you hide hydrogens using the **View** menu, both locked hydrogen atoms, and atoms with unsatisfied valence, will remain displayed.

You can also choose to display a warning message if you attempt to save a chemical sample file that contains non-standard hybridization or unsatisfied valence.

Changing view settings for hydrogens and electrons

To display locked hydrogen atoms and hydrogens attached to atoms with unsatisfied valence

1. Choose **Options** | **Valence Settings** to display the Valence Settings dialog box.



2. Select the **Show locked hydrogen atoms and those attached to atoms with unsatisfied valence** check box so that it is enabled.
3. Select **OK** to close the Valence Settings dialog box and to save the view setting for hydrogens.

To display hydrogens not bonded to carbon atoms

1. Choose **Options | Valence Settings** to display the Valence Settings dialog box.
2. Select the **Suppress hydrogens not bonded to carbon atoms** check box so that it is not checked.
3. Select **OK** to close the Valence Settings dialog box and to save the view setting for hydrogen atoms.

   This setting applies only when **View | Suppress Hydrogens** is checked. In that case, all hydrogen atoms bonded to carbon are hidden and only those atoms attached to other elements are displayed. If **View | Suppress Hydrogens** is not checked, all hydrogen atoms are displayed.

To display electrons attached to atoms with unsatisfied valence

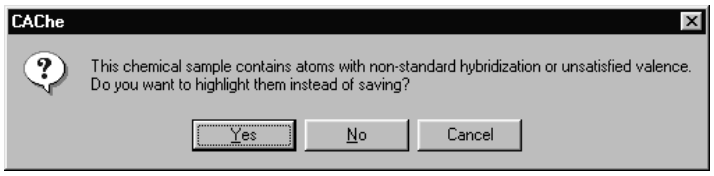
1. Choose **Options | Valence Settings** to display the Valence Settings dialog box.
2. Select the **Show electrons attached to atoms with unsatisfied valence** check box so that it is enabled.
3. Select **OK** to close the Valence Settings dialog box and to save the view setting for electrons.

To display a warning when saving files containing non-standard hybridization or unsatisfied valence

1. Choose **Options | Valence Settings** to display the Valence Settings dialog box.
2. Select the **When saving files, display warning for any atoms with non-standard hybridization or unsatisfied valence** check box so that it is enabled.
3. Select **OK** to close the Valence Settings dialog box.

   When you attempt to save a chemical sample file containing atoms with non-standard hybridization or unsatisfied valence, an

alert box is displayed.



4. Do one of the following:
   - Select **Yes** to highlight atoms with non-standard hybridization or unsatisfied valence.
   - Select **No** to save the chemical sample file without highlighting atoms with non-standard hybridization or unsatisfied valence.
   - Select **Cancel** to close the alert box.

Saving settings

When you change the display styles for atoms and bonds, the changes only apply to selected objects in the active workspace, unless you specify that you want to make that display style a default setting.

Once you have made a display style the default, any new atoms or bonds added to an existing chemical sample file or to a new chemical sample file will be displayed in the new default style.

📖 NOTE When you change default settings, those default settings will not apply to display styles for atoms and bonds in chemical sample files that you have already saved. Default settings only apply to atoms and bonds you draw after changing the default settings.

Changing settings using menu options

The following settings become default settings as soon as you change them:

- **View** | **Suppress Hydrogens**
- **View** | **Show Electrons**



Refer to *"Hiding atoms"*, p 6-18, and *"Changing the appearance of atoms"*, p 6-8, for information on these **View** menu options.

- **Options** | **Use Faster Motion**



Refer to Chapter 7, *"Manipulating Molecules"*, for information on this **Options** menu option.

- **Adjust** | **Enable Locks**



Refer to Chapter 7, *"Manipulating Molecules"*, for information on this **Adjust** menu option.

- all settings in the Periodic Table Settings dialog box, displayed by choosing **Options** | **Periodic Table Settings**



Refer to the following for information on this **Options** menu option:

"Changing view settings", p 6-37.

Chapter 4, *"Creating Chemical Samples"*.

Chapter 5, *"Modifying Chemical Samples"*.

Changing settings using a dialog box

The following settings become default settings by selecting **Make Default** in the relevant dialog box:

- all colors in the Define Colors dialog box color palette, displayed by choosing **View** | **Color Palette**



Refer to *"Changing view settings"*, p 6-37, for information on this **View** menu option.

- all settings in the Atom Attributes dialog box, displayed by choosing **View** | **Atom Attributes**



Refer to *"Changing the appearance of atoms"*, p 6-8, for information on this **View** menu option.

- all settings in the Bond Attributes dialog box, displayed by choosing **View** | **Bond Attributes**



Refer to *"Changing the appearance of bonds"*, p 6-21, for information on this **View** menu option.

- all settings in the Geometry Label Attributes dialog box, displayed by choosing **View** | **Geometry Label Attributes**



Refer to Chapter 8, *"Investigating Molecular Geometry"*, for information on this **View** menu option.

- all settings in the Surface Attributes dialog box, displayed by choosing **Analyze** | **Surface Attributes**


Refer to *"Viewing a surface"*, p 15-9, for information on this **View** menu option.

- all settings in the Select Similar Settings dialog box, displayed by choosing **Options** | **Select Similar Settings**


Refer to Chapter 5, *"Modifying Chemical Samples"*, for information on this **Options** menu option.

- all settings in the Drawing Settings dialog box, displayed by choosing **Options** | **Drawing Settings**


Refer to *"Changing view settings"*, p 6-37, for information on this **Options** menu option.

- all settings in the Rotation Settings dialog box, displayed by choosing **Options** | **Rotation Settings**


Refer to Chapter 7, *"Manipulating Molecules"*, for information on this **Options** menu option.

- all settings in the View Settings dialog box, displayed by choosing **Options** | **View Settings**


Refer to "Changing view settings" earlier in this chapter for information on this **Options** menu option.

- all settings in the Valence Settings dialog box, displayed by choosing **Options** | **Valence Settings**


Refer to *"Changing view settings"*, p 6-37, for information on this **Options** menu option.

Building crystal structures

CAChe enables you to build models of infinite lattice and molecular crystal structures within the workspace.

CAChe enables you to:

- select a space group
- define cell parameters
- define fractional coordinates of the asymmetric atoms
- build a structure containing only the asymmetric atoms and bonds
- build the molecular structure from asymmetric atoms, which can then be used to build a molecular crystal
- build an infinite lattice
- display and hide crystal boundaries
- open CrystalStructure and ShelX file types
- import data from a text file into the Crystal Shape dialog box.

There are five ways that you can add asymmetric atoms, from which the crystal structure is built:

- add atoms to a workspace using the Atom tool

Refer to *"Using the Atom/Bond tool"*, p 4-4 for further details.

- add atoms to a workspace by opening a chemical sample file

Refer to *"Working with chemical sample files"*, p 4-2 for further details.

- use the Crystal Shape dialog box to enter the atomic symbols and their fractional coordinates
- create an ASCII text file of data using a specified file format; when you open this file, the asymmetric atoms and bonds are added to the workspace

- copy data from a text file and paste it into a fractional coordinates table.

From the asymmetric atoms, space group, and unit cell parameters, the necessary transformations are performed to create the unit cell. You specify the number of times the unit cell is repeated in three dimensions to build the crystal structure.

Selecting a space group

When you select a space group, you are choosing the transform used to build the crystal from asymmetric atoms.

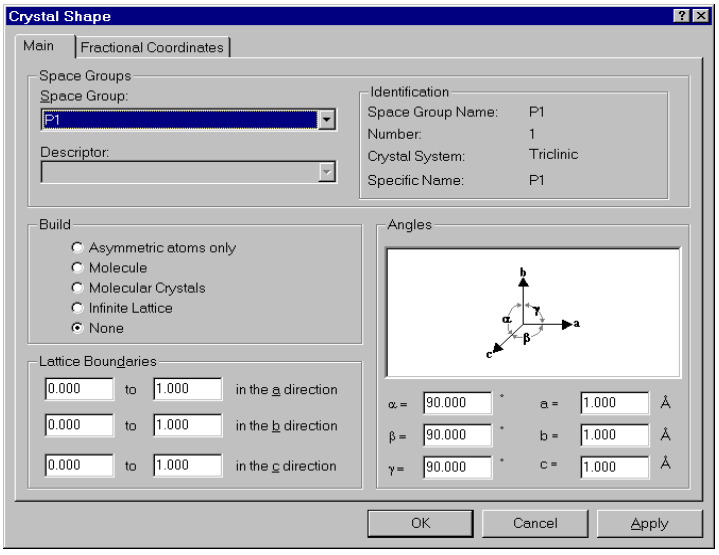
The choice of space group includes:

- short International (Hermann-Mauguin) space group symbols
- common abbreviated names (specific names)

  for the alternate symbols of monoclinic space groups.

To select a space group

1. Select the crystal structure that you want to change by clicking on it with the Select Molecule Tool.
2. Choose **Edit | Crystal Shape** to display the Crystal Shape dialog box.



3. In the **Space Groups** panel, select the arrow button in the **Space Group** box and choose a group from the drop-down list.

   The complete identification for that space group is displayed in the **Identification** panel of the dialog box.

   The space group name and number, the crystal system to which it belongs, and the specific name are shown. The associated **Descriptor** is displayed.

4. If the space group has more than one descriptor, select the arrow button in the **Descriptor** box and choose the one that you require.

   The **Descriptor** drop-down list is grayed out if there are no choices available for the space group you selected.

5. Select **Apply** to view the crystal structure in the workspace.

6. Select **OK** to accept the changes and to close the Crystal Shape dialog box.

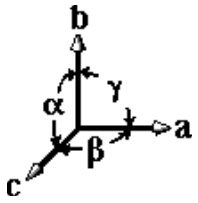
Space group symbols found elsewhere have equivalent space group nomenclature in CAChe. The following table identifies the short International space groups used by CAChe that are equivalent to other published symbols. Find the alternative space group nomenclature used in the literature in the column on the right to identify the CAChe equivalent nomenclature on the left.

CAChe	Alternative	CAChe	Alternative
Pmm2	Pmm	Imm2	Imm
$Pmc2_1$	Pmc	Iba2	Iba
Pcc2	Pcc	Ima2	Ima
Pma2	Pma	$P4_2cm$	P4cm
$Pca2_1$	Pca	$P4_2nm$	P4nm
Pnc2	Pnc	$P4_2mc$	P4mc
$Pmn2_1$	Pmn	$P4_2bc$	P4bc
Pba2	Pba	$I4_1md$	I4md
$Pna2_1$	Pna	$I4_1cd$	I4cd
Pnn2	Pnn	$P4_2mmc$	P4/mmc
Cmm2	Cmm	$P4_2mcm$	P4/mcm
$Cmc2_1$	Cmc	$P4_2nbc$	P4/nbc
Ccc2	Ccc	$P4_2nnm$	P4/nnm
Amm2	Amm	$P4_2mbc$	P4/mbc
Abm2	Abm	$P4_2mnm$	P4/mnm
Ama2	Ama	$P4_2nmc$	P4/nmc
Aba2	Aba	$I4_1/amb$	I4/amd
Fmm2	Fmm	$I4_1/acd$	I4/acd

CAChe	Alternative	CAChe	Alternative
Fdd2	Fdd	P622	C62
P3	C3	$P6_122$	$C6_12$
$P3_1$	$C3_1$	$P6_522$	$C6_52$
$P3_2$	$C3_2$	$P6_222$	$C6_22$
P-3	C-3	$P6_422$	$C6_42$
P312	C312	$P6_322$	$C6_32$
P321	C32	P6mm	C6mm
$P3_112$	$C3_112$	P6cc	C6cc
$P3_121$	$C3_12$	$P6_3cm$	$C6_3cm$
$P3_212$	$C3_212$	$P6_3mc$	$C6_3mc$
$P3_221$	$C3_22$	P-6m2	C-6m
P3m1	C3m	P-6c2	C-6c
P31m	C31m	P-62m	C-62m
P3c1	C3c	P-62c	C-62c
P31c	C31c	P6/mmm	C6/mmm
P-31m	C-31m	P6/mcc	C6/mcc
P-31c	C-31c	$P6_3/mcm$	C6/mcm
P-3m1	C-3m	$P6_3/mmc$	C6/mmc
P-3c1	C-3c	P432	P43
P6	C6	$P4_232$	$P4_23$
$P6_1$	$C6_1$	F432	F43
$P6_5$	$C6_5$	$F4_132$	$F4_13$
$P6_2$	$C6_2$	I432	I43
$P6_4$	$C6_4$	$P4_332$	$P4_33$
$P6_3$	$C6_3$	$P4_132$	$P4_13$
P-6	C-6	$I4_132$	$I4_13$
P6/m	C6/m		
$P6_3/m$	$C6_3/m$		

Defining cell parameters

Cell parameters define the unit cell for the space group. The cell parameters a, b, and c specify the lengths of the edges of the unit cell, and the cell parameters α, β, and γ specify the angles between the edges of the unit cell.



To define cell parameters

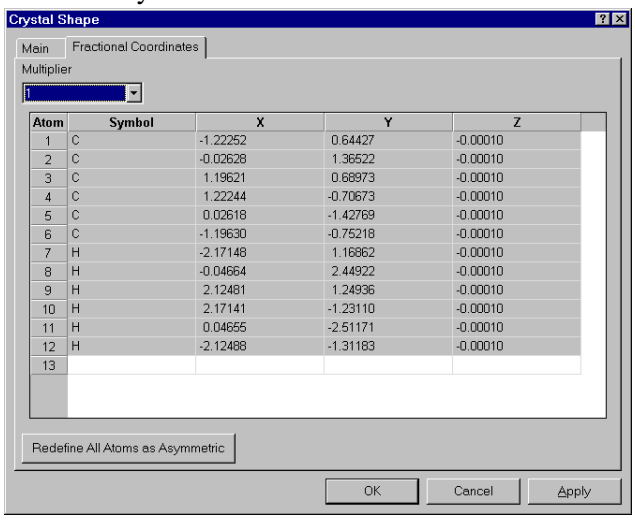
1. Select the crystal structure using the Select Molecule Tool.
2. Choose **Edit | Crystal Shape** to display the Crystal Shape dialog box.
3. In the **Angles** panel, enter values by editing the **a=**, **b=**, **c=**, and α**=**, β**=**, γ**=** text boxes.

   If the crystal system to which the space group belongs places restraints on unit cell parameters, values for the cell parameters will be automatically entered.
4. Select **Apply** to view the crystal structure in the workspace.
5. Select **OK** to accept the changes and to close the Crystal Shape dialog box.

Defining fractional coordinates

You can use the Fractional Coordinates tab of the Crystal Shape dialog box to:

- enter asymmetric atoms and their fractional coordinates before you build a crystal
- enter and edit atoms and their fractional coordinates after you build a crystal.



To define the fractional coordinates

NOTE If you are entering asymmetric atoms before you build the crystal, enter the space group and cell parameters first.

1. Choose **Edit | Crystal Shape** to display the Crystal Shape dialog box.
2. Select the **Fractional Coordinates** tab.
3. Select the arrow button in the **Multiplier** box, and choose a value from the drop-down list.

   The multiplier divides the entered coordinates to give the fractional coordinates.
4. In the **Symbol** column, do one of the following:
   - enter the atomic symbol for each atom
   - enter an alphanumeric label, containing an atomic symbol and any numeric tag, to uniquely identify each asymmetric atom.

   Each atom in the crystal is assigned a unique number that is displayed in the **Atom** column.
5. Enter the coordinates in the **X**, **Y**, and **Z** columns by clicking the left uppermost cell using the **left** mouse button, and use the **Tab** key to move between cells.
6. Select **Redefine All Atoms as Asymmetric** to identify additional atoms as asymmetric.
7. Select **Apply** to view the crystal structure in the workspace.
8. Select **OK** to accept the structure and to close the Crystal Shape dialog box.

The fractional coordinates are altered when you use CAChe computational methods, or use commands in the workspace Beautify menu, on the crystal structure.

You can transfer data between tables on the Fractional Coordinates tab using **Edit | Copy** and **Edit | Paste**.

Building asymmetric atoms

You may want to build only the asymmetric atoms. This option can be used after building a molecular crystal or infinite lattice as a way to start again. This option deletes all bonds and all atoms except asymmetric atoms from the molecule file.

To build asymmetric atoms

1. Select the crystal structure using the Select Molecule Tool.
2. Choose **Edit | Crystal Shape** to display the Crystal Shape dialog box.
3. In the **Build** panel, select **Asymmetric atoms only**.
4. Select **Apply** to view the crystal structure in the workspace.

   The asymmetric atoms are displayed, and you can edit their positions.
5. Select **OK** to accept the changes and to close the Crystal Shape dialog box.

Building a molecular crystal

You can build a molecular crystal by first building one molecule from asymmetric atoms. This enables you to adjust bond types in the molecule before you build the molecular crystal.

To build a molecule

1. Choose **Edit | Crystal Shape** to display the Crystal Shape dialog box.
2. Define the space group and cell parameters in the **Space Group** panel and **Angles** panel, respectively.
3. In the **Build** panel, select **Molecule**.
4. Select the **Fractional Coordinates** tab.
5. In the **Symbol** column, do one of the following:
   - enter the atomic symbol for each atom
   - enter an alphanumeric label, containing an atomic symbol and

any numeric tag, to uniquely identify each asymmetric atom.

6. Enter the coordinates in the **X**, **Y**, and **Z** columns by clicking the left uppermost cell using the **left** mouse button, and use the **Tab** key to move between cells.
7. Select **Apply** to view the crystal structure in the workspace.

   The bond types and atom configuration can be corrected if necessary. You can also add structures, such as water molecules, before building the molecular crystal.
8. Select **OK** to accept the changes and to close the Crystal Shape dialog box.

To build a molecular crystal

1. Select the crystal structure using the Select Molecule Tool.
2. Choose **Edit | Crystal Shape** to display the Crystal Shape dialog box.
3. In the **Build** panel, select **Molecular Crystals**.
4. Select **Apply** to view the structure in the workspace.
5. Select **OK** to accept the changes and to close the Crystal Shape dialog box.

   The molecular crystal is built using the bonds present in the workspace and the asymmetric atoms. If no bonds are present, the crystal is built using a formula that estimates bond lengths according to covalent radii and electronegativity.

According to this formula, when the distance between two atoms is less than the estimated bond length, they are considered bonded. Bond types are then assigned depending on the types of atoms and the distance between them. If atoms are closer than one-half the normal bond length, they are considered too close and no bond is formed. After the molecule is built from asymmetric atoms using this bond formation formula, the molecular crystal is built.

Building an infinite lattice

You can build an infinite lattice crystal by entering the fractional coordinates of the asymmetric atoms.

To build an infinite lattice

1. Choose **Edit | Crystal Shape** to display the Crystal Shape dialog box.
2. Select the **Fractional Coordinates** tab, and enter the fractional coordinates of asymmetric atoms.
3. Select the **Main** tab.
4. Choose the appropriate **Space Group** from the drop-down list.
5. Enter the cell parameters using the **Angles** panel.
6. In the **Build** panel, select **Infinite Lattice**.
7. Select **Apply** to view the infinite lattice in the workspace.

   Bonds are based on the distance criteria as molecular crystals. Infinite lattices are trimmed to lattice boundaries.
8. Select **OK** to accept the changes and to close the Crystal Shape dialog box.

To change the lattice boundaries

1. Select the infinite lattice using the Select Molecule Tool.
2. Choose **Edit | Crystal Shape** to display the Crystal Shape dialog box.
3. In the **Lattice Boundaries** panel, enter the lattice boundaries in both positive and negative a, b, and c directions.
4. Select **Apply** to view the changes in the workspace.

   The size of the crystal is changed accordingly.
5. Select **OK** to accept the changes and to close the Crystal Shape dialog box.

Displaying and hiding crystal boundaries

You can display or hide outlines of the asymmetric cell, unit cell, and crystal lattice.

📖 NOTE To enable the display of crystal boundaries, the structure requires crystal information first: display the Crystal Shape dialog box, and select either **OK** or **Apply**.

To display the asymmetric cell

1. Select the asymmetric atom using the Select Tool.
2. Choose **Edit | Crystal Boundaries | Draw Asymmetric Cell**.

   An outline of the asymmetric cell is displayed.

To display the unit cell

1. Select the asymmetric atom using the Select Tool.
2. Choose **Edit | Crystal Boundaries | Draw Unit Cell**.

   An outline of the unit cell is displayed.

To display the lattice boundaries

1. Select the asymmetric atom using the Select Tool.
2. Choose **Edit | Crystal Boundaries | Draw Lattice Boundaries**.

   An outline of the crystal lattice is displayed.

Creating CrystalStructure files

You can build crystal structures by opening a CrystalStructure file. A CrystalStructure file is an ASCII text file that you create with a word processing application. This file enables you to enter fractional coordinates and thermal tensor parameters for atoms derived from theoretical or experimental data.

CrystalStructure files have the following format and information:

Line #	format
1	CrystalStructure (spelled exactly as shown)
2	Comments (must be present)
3	Comments (must be present)
4	Comments (must be present)
5	a = {length of a axis in angstroms}
6	b = {length of b axis in angstroms}
7	c = {length of c axis in angstroms}
8	alpha = {angle in degrees}
9	beta = {angle in degrees}
10	gamma = {angle in degrees}
11	scale = {multiplier converting *x, y, z* coordinates to range (0,1)
12	Repeat cell = {number of times to repeat the unit cell along a, b and c axes}
13	Space Group = {international space group symbol}
14	Descriptor = none {or enter the descriptor as found on the third line of the International Tables for Crystallography}
15	Temperature Factor = (must be UIJ, BIJ, or BETA) {This line is optional}
16	Z x y z T11 T22 T33 T12 T13 T23 {Z=the atomic symbol or atom label; x, y, z = fractional coordinates, separated by tabs or white space; T## = optional thermal tensor data separated by tabs or white space. Parentheses () can be used to include additional comments; data enclosed in parentheses are ignored.}

Note the following:

- The CrystalStructure file can have any name, but the first line in the file must include the word `CrystalStructure` spelled exactly as shown.
- Three comment lines must follow. The keywords are case sensitive and should be spelled exactly as shown.
- Thermal tensor data is optional. If only the first element of the tensor is entered, then the atom is considered isotropic.

To build a crystal structure using a CrystalStructure file

1. Choose **File | Open** to display the Open dialog box.
2. From the **Files of type** drop-down list select **Crystal Structure (*.xsf)**.
3. Select the file.
4. From the scrolling list, locate the file and click on it to select it.
5. Select **Open** to open the CrystalStructure file.

   The crystal structure is displayed in the workspace.

If you entered thermal tensor data into the CrystalStructure file, you can build a crystal and represent atoms as thermal ellipsoids using the **Thermal Ellipsoid** command in the **Shape** tab of the **Atom Attributes** dialog box.

Refer to *"Changing atom shape"*, p 6-11, for further information.

ShelX files

You can build crystal structures by opening a ShelX Instruction file.

To open a ShelX Instruction file

1. Choose **File | Open** to display the Open dialog box.
2. From the **Files of type** drop-down list select **ShelX Instruction (*.ins)**.
3. Select the file.
4. From the scrolling list, locate the file and click on it to select it.
5. Select **Open** to open the ShelX file.

   The structure displays asymmetric atoms lacking bonds. Information about fractional coordinates, the space group, and descriptors are included in the file. This enables you to easily reconstruct the original crystal using the Crystal Shape dialog box.

If you entered thermal tensor data into the ShelX file, you can build a crystal and represent atoms as thermal ellipsoids using the **Thermal Ellipsoid** command in the **Shape** tab of the **Atom Attributes** dialog box.

Refer to *"Changing atom shape"*, p 6-11, for further information.

Importing data from a text file

Data may be copied from text files, *via* the clipboard, into the fractional coordinates table of the Crystal Shape dialog box.

To import data from a text file

1. Open the file using a text editor.
2. Select the rows you want to copy, and copy the data to your clipboard by pressing **Ctrl C**.
3. Choose **Edit | Crystal Shape** to open the Crystal Shape dialog box.
4. Select the **Fractional Coordinates** tab.
5. Select one or more rows by clicking on a row in the **Atom** column and holding down the **Shift** key.
6. Press **Ctrl V** to paste the data from your clipboard to the table.
7. Select **Apply** to view the structure in the workspace.
8. Select **OK** to accept the changes and to close the Crystal Shape dialog box.

7 Manipulating Molecules

Overview

This chapter describes how to manipulate molecules in the CAChe workspace, including how to:

- use the manipulation tools to rotate, translate, and scale workspace objects
- rotate, translate, and scale only selected portions of your molecule
- duplicate, copy, cut, delete, and paste selected portions of your molecule
- superimpose one molecule over another to visualize geometrical differences
- fuse atoms and bonds from one cyclic structure with atoms and bonds from another cyclic structure
- name and define groups of atoms
- select atom groups and portions of atom groups.

Contents

Using the manipulation tools **7-2**
Using the Rotate tool 7-3
Using the Translate tool 7-5
Using the Scale tool 7-8
Manipulating portions of your molecule **7-9**
Using faster motion mode **7-12**
Duplicating molecules **7-13**
Duplicating workspace objects 7-13
Copying workspace objects 7-14
Copying objects from ChemDraw or ISIS Draw 7-17
Deleting portions of your molecule **7-18**
Cutting workspace objects 7-18
Deleting workspace objects 7-19
The undo command 7-19
Fusing ring structures **7-21**
Grouping atoms **7-24**
Defining a group 7-24
Selecting groups and portions of groups 7-25
Changing atom order in groups 7-28
Showing residues in Group Atoms dialog box 7-29

Using the manipulation tools

The CAChe workspace tools allow you to move your chemical sample around the workspace in a variety of ways, enabling you to view its properties and spatial geometry more clearly.

The workspace tool palette provides you with the following three manipulation tools:

- the Rotate tool, which rotates objects in two or three dimensions around the workspace x, y, and z axes
- the Translate tool, which moves objects around the workspace in two dimensions
- the Scale tool, which zooms into and out from a workspace object.

Select a tool by clicking on it in the tool palette. When you select a tool, the mouse cursor in the workspace changes shape to indicate which tool is currently selected. The table below shows the three manipulation tools and their corresponding mouse cursors:

Manipulation tool	Tool palette icon	Mouse cursor
• the Rotate tool		
• the Translate tool		
• the Scale tool		

📖 NOTE When you use the manipulation tools, all objects in the workspace are rotated, translated, or scaled.
To rotate, translate, and scale selected objects only, choose **Edit | Move Selected** to enter position mode. Refer to *"Manipulating portions of your molecule"*, p 7-9, for more information.

Using the Rotate tool

Rotating a chemical sample with the Rotate tool mimics the movement of the chemical sample in the x, y, and z directions. When you first draw a molecule and rotate it, the rotation is centered around the center of the workspace; i.e., around the origin of the workspace's three-dimensional coordinate system. You can alter the center of rotation to the center of a currently selected object. This is described in the section *"Defining the center of rotation"*, p 7-4.



Use the Rotate tool to:

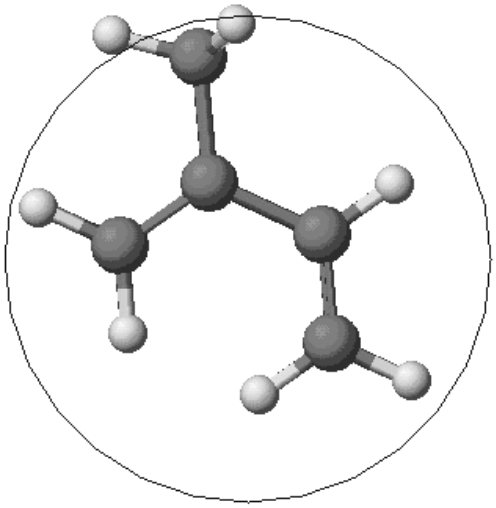
- rotate workspace objects around the x and y axes
- rotate workspace objects around the z axis.

To select the Rotate tool



1. Select the Rotate tool by clicking on it in the tool palette.
2. The mouse cursor changes to the Rotate tool, shown to the left.

   A black circle is displayed in the center of the workspace, as shown in the following example.



Rotating objects around the x and y axes

To rotate workspace objects around the x and y axes

1. Position the Rotate tool inside the black circle in the workspace.
2. Click and drag in the workspace to the left and right with the Rotate tool.

   Workspace objects are rotated around the y axis.
3. Click and drag up and down in the workspace with the Rotate tool.

   Workspace objects are rotated around the x axis.
4. Click and drag up and down diagonally in the workspace with the Rotate tool.

   Workspace objects are rotated around the x and y axes.

Rotating objects around the z axis

To rotate workspace objects around the z axis

1. Position the Rotate tool outside of the black circle in the workspace.
2. Click and drag in the workspace to the left or down with the Rotate tool.

   Workspace objects are rotated around the z axis in a clockwise direction.
3. Click and drag in the workspace to the right or up with the Rotate tool.

   Workspace objects are rotated around the z axis in an anti-clockwise direction.

Defining the center of rotation

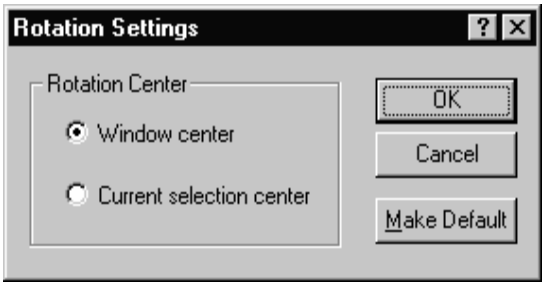
You can control the operation of the Rotate tool by changing the center of rotation about which the tool operates.

Center rotation around:

- the center of the workspace
- the center of currently selected objects.

To define the center of rotation for the Rotate tool

1. Choose **Options** | **Rotation Settings** to display the Rotation Settings dialog box.



2. To rotate workspace objects around the center of the workspace, select the **Window Center** radio button so that it is enabled.
3. To rotate workspace objects around the center of any currently selected object, select the **Current Selection Center** radio button so that it is enabled.
4. Select **OK** to close the Rotation Settings dialog box and to save the rotation settings for the Rotate tool.

Using the Translate tool

The Translate tool allows you to move the chemical sample sideways and up and down in the workspace relative to the x and y coordinates of the workspace.



Use the Translate tool to:

- move workspace objects around the workspace.



Refer to *"Other ways to move workspace objects"*, p 7-7, for further details about moving your molecule and its components around the workspace.

To select the Translate tool

1. Select the Translate tool by clicking on it in the tool palette.
2. The mouse cursor changes to the Translate tool, shown to the left.



Moving objects around the workspace

To move workspace objects relative to the x and y axes

1. Position the Translate tool anywhere in the workspace.
2. Click and drag with the Translate tool in the direction that you want to move workspace objects.

   For example, to move your chemical sample to the bottom of the workspace, click and drag downwards.

   Workspace objects are moved in the direction that you drag the Translate tool.

Recentering workspace objects

When you use the Translate tool, workspace objects move away from the center of the workspace. This means that the next time you rotate your chemical sample using the Rotate tool, your chemical sample rotates in an arc around the x, y, or z axes, instead of rotating around its center.

It is possible to translate a molecule so far from the center of the workspace that when you rotate it, the molecule's motion takes it off the edge of the screen.

You can return your molecule to the center of the workspace or resize it to fit the workspace window to recover workspace objects that have disappeared from view.

Centering workspace objects

You can center selected portions of your chemical sample in the workspace window. The size of the selected objects is not changed.

To center objects in the workspace

1. Select the workspace object that you want to center by clicking on it with a selection tool.

   The object is highlighted to show that it is selected.

2. Choose **View | Center in Window**.

   The selected workspace object is moved to the center of the workspace.

Scaling and centering workspace objects

You can center selected portions of your chemical sample in the workspace and scale the selected portion so that it fits into the currently sized workspace.

To scale and center objects in the workspace

1. Select the workspace object that you want to center and scale relative to the size of the workspace window by clicking on the object with a selection tool.

   The object is highlighted to show that it is selected.

2. Do one of the following:

   - Choose **View | Fit in Window**
   - Select the toolbar button shown to the left.

   - Press **Ctrl F**

   The selected workspace object is rescaled and moved to the center of the workspace.

Other ways to move workspace objects

Apart from using the Translate tool, you can also move workspace objects by:

- selecting one or more objects with a selection tool, and dragging across the workspace

  The selected objects move to the location to which you dragged the selection tool.

- using geometry labels to accurately adjust the geometrical relationship between atoms in the workspace.

Refer to Chapter 8, *"Investigating Molecular Geometry"*, for more information on geometry labels and how to adjust them.

Using the Scale tool



Scaling lets you zoom into and out from workspace objects along the z axis of the workspace.

To select the Scale tool



1. Select the Scale tool by clicking on it in the tool palette.

   The mouse cursor changes to the Scale tool, shown to the left.

Zooming in and out on workspace objects

To zoom in and out on workspace objects

1. Position the Scale tool anywhere in the workspace.
2. Click and drag with the Scale tool to the right or upwards in the workspace to zoom in on workspace objects.

   Workspace objects increase in size as you drag the Scale tool.
3. Click and drag with the Scale tool to the left or downwards in the workspace to zoom out from workspace objects.

   Workspace objects decrease in size as you drag the Scale tool.

Manipulating portions of your molecule

When you use the manipulation tools in the way described in the previous section, *"Using the manipulation tools"*, all objects present in the workspace are rotated, translated, or scaled. CAChe also allows you to manipulate selected portions of your molecule, while the remainder of the workspace objects remain stationary.

Using position mode, you can rotate, translate, or scale selected portions of your chemical sample. This enables you to carry out tasks such as positioning selected fragments for bonding, or rotating selected functional groups to visualize individual properties more clearly.

The changes you make to atom positions while in position mode actually change the x, y, and z coordinates of molecular components. Because of this, use caution when scaling objects in position mode. Scaling selected portions of a chemical sample can result in:

- abnormally strained bond distances
- an unreasonable molecular geometry that produces meaningless energy values in CAChe experiments.

CAChe displays a warning message if you attempt to scale selected portions of your chemical sample while in position mode.

To manipulate selected workspace objects

1. Select the atoms and bonds that you want to rotate, translate, or scale by clicking on them with a selection tool.

   The selected atoms and bonds are highlighted to show that they are selected.

2. Do one of the following to enter position mode:

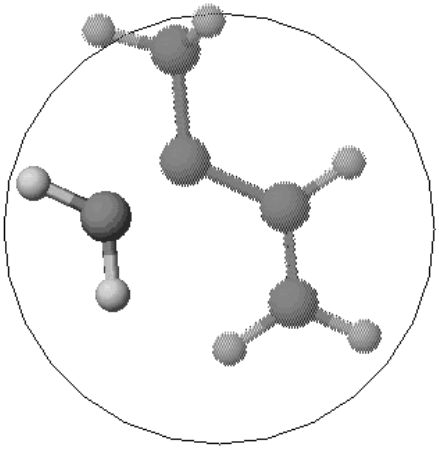
   

   - Choose **Edit** | **Move Selected**
   - Select the toolbar button shown to the left.

   A check mark is displayed next to the **Move Selected** drop-down list option to indicate that you are in position mode.

   The Rotate tool is automatically enabled and the cursor changes to the Rotate tool. A black circle is displayed in the center of the

workspace. The selected atoms and bonds are displayed as a separate group from the rest of the molecule, with all connecting bonds temporarily hidden. An example is shown below.



3. To rotate the selected object, click and drag the Rotate tool inside the black circle to rotate the object along the x and y axes, or outside of the black circle to rotate the object along the z axis.
4. To translate the selected object, use the Translate tool to click and drag the cursor to the workspace location where you want to put the selected object.
5. To scale the selected object, use the Scale tool to zoom into or out from the selected object.

   When you select the Scale tool by clicking on it in the tool palette, a warning message is displayed, informing you that scaling a portion of your chemical sample will affect atom distances.

   Do one of the following:

   - Select **OK** to proceed and select the Scale tool.
   - Select **Cancel** to return to using the Rotate or Translate tool.

   If you select **OK**, click and drag the Scale tool to zoom into and out from the selected object.
6. Do one of the following to exit position mode:

   - Select a selection tool or the Atom/bond tool by clicking on

the tool in the tool palette.

- Choose any menu option.

The check mark next to the **Move Selected** drop-down list option disappears.

Using faster motion mode

Faster motion mode is helpful when viewing or manipulating large structures in the workspace. When you make a change to your chemical sample or manipulate it in some way, the chemical sample appears in a simplified form such as a line drawing. This increases the speed at which CAChe can redraw the moving or changing molecule.

As soon as the simplified display of the molecule is complete, CAChe reverts to the current display mode. For example, if you have chosen to view your chemical sample in ball and cylinder mode, the molecule reverts back from a line drawing into a ball and cylinder model.

If you further manipulate or change a molecule before CAChe can reapply the current display style, the chemical sample remains in its simplified line drawing mode, so speeding up the rate of screen display for the molecule.

To use faster motion mode

1. Choose **Options** | **Use Faster Motion**.

   A check mark is displayed next to the drop-down list option to indicate that faster motion mode is enabled.

   Objects in the workspace are temporarily displayed as a line drawing when you next perform a manipulation or editing action on your chemical sample.

   When you complete the manipulation or editing of your chemical sample, the display style reverts to the currently chosen mode.

Duplicating molecules

If your molecule includes fragments that are repeated, you can build the fragment once and copy it. In CAChe, you can either duplicate an object, or copy and paste it.

Duplicating workspace objects

When you duplicate an object, the new copy of the object is offset from the original object slightly and becomes the only object selected. You can then manipulate the newly duplicated structure into a new location by using position mode.

The contents of the Windows Clipboard is not affected by duplicating an object.

To duplicate an object

1. Select the object that you want to duplicate by clicking on it with a selection tool.

   The object is highlighted to show that it is selected.

2. Do one of the following:

   - Choose **Edit** | **Duplicate**
   - Press **Ctrl D**.

   A copy of the selected object is displayed in the workspace, above and to one side of the original object. The copy is highlighted in the workspace to show that it is selected, while all other workspace objects are grayed out.

3. Do one of the following:

   - Click and drag in the workspace with a selection tool to move the selected copy to the location you want.
   - Click and drag the Translate tool across the workspace to the location where you want to place the duplicated object.

   The duplicate moves to the location where you dragged it.

Copying workspace objects

You can copy any selected object to the Windows Clipboard and paste it into the active workspace or into a different workspace. When you paste an object, it appears as a selected object in the center of the workspace. You can paste the same object repeatedly.

You can also copy and paste a workspace object into another Windows application, for example ChemDraw/ISIS Draw. The image is pasted as a Windows bitmap.

To copy and paste an object in the active workspace

1. Select the object that you want to copy by clicking on it with a selection tool.

   The object is highlighted to show that it is selected.

2. Do one of the following:
   - Choose **Edit** | **Copy**.
   - Press **Ctrl C**.
   - Select the toolbar button shown to the left.



3. Do one of the following:
   - Choose **Edit** | **Paste**.
   - Press **Ctrl V**.
   - Select the toolbar button shown to the left.



   A copy of the selected object is pasted in the center of the active workspace. The copy is highlighted in the workspace to show that it is selected, while all other workspace objects are grayed out.

4. Do one of the following:
   - Click and drag in the workspace with a selection tool to move the selected copy to the location you want.
   - Use the Translate tool to click and drag across the workspace to the location where you want to place the copied object.

   The pasted copy moves to the location where you dragged it.

The copied object remains on the Windows Clipboard until you copy or cut another object, or quit CAChe, so you can continue to paste copies of the object until you have the required number of copies.

To copy and paste an object to another workspace

1. Select the object that you want to copy by clicking on it with a selection tool.

   The object is highlighted to show that it is selected.

2. Do one of the following:
   - Choose **Edit** | **Copy**.
   - Press **Ctrl C**.
   - Select the toolbar button shown to the left.



3. Do one of the following:
   - Choose **File** | **Open** to open the chemical sample file in which you want to paste the copied object.
   - If the chemical sample file in which you want to paste the copied object is already open, click on its workspace to make it active.
4. Do one of the following:
   - Choose **Edit** | **Paste**.
   - Press **Ctrl V**.
   - Select the toolbar button shown to the left.



   A copy of the selected object is pasted in the center of the active workspace. The copy is highlighted in the workspace to show that it is selected, while all other workspace objects are grayed out.
5. Do one of the following:
   - Click and drag in the workspace with a selection tool to move the selected copy to the location you want.
   - Use the Translate tool to click and drag across the workspace to the location where you want to place the copied object.

   The pasted copy moves to the location where you dragged it.

The copied object remains on the Windows Clipboard until you copy or cut another object, or quit CAChe, so you can continue to paste copies of the object until you have the required number of copies.

To copy and paste an object to another Windows application

1. Select the object that you want to copy by clicking on it with a selection tool.

   The object is highlighted to show that it is selected.

2. Do one of the following:

   - Choose **Edit** | **Copy**.
   - Press **Ctrl C**.
   - Select the toolbar button shown to the left.



3. Open or maximize the application in which you want to paste the copied object.
4. Open or select the document into which you want to paste the copied object.
5. Do one of the following:

   - Choose **Edit** | **Paste**.
   - Press **Ctrl V**.

   An image of the selected object is pasted into the document in the format of a Windows bitmap.

   The copied object remains on the Windows Clipboard until you copy or cut another object, or quit CAChe, so you can continue to paste copies of the object until you have the required number of copies.

Copying objects from ChemDraw or ISIS Draw

You can copy any selected object to the Windows Clipboard from ChemDraw or ISIS Draw, and paste it into the workspace.

To copy and paste an object from ChemDraw or ISIS Draw

1. Select the object that you want to copy by clicking on it with a selection tool.
2. Do one of the following:
   - Choose **Edit | Copy**
   - Press **Ctrl C**
3. Do one of the following:
   - Choose **File | Open** to open the chemical sample file in which you want to paste the copied object.
   - If the chemical sample file in which you want to paste the copied object is already open, click on its workspace to make it active.

NOTE CACHe only transfers chemical samples smaller than 400 atoms to ChemDraw and IsisDraw. To transfer information to ChemDraw or IsisDraw, CACHe places an SD file on the clipboard. The largest chemical sample that can be placed on the clipboard in SD format is 400 atoms.

4. Do one of the following:
   - Choose **Edit | Paste**.
   - Press **Ctrl V**.

   A copy of the selected object is pasted in the center of the active workspace. The copy is highlighted in the workspace to show that it is selected, while all other workspace objects are grayed out.

   The copied object remains on the Windows Clipboard until you copy or cut another object, so you can continue to paste copies of the object until you have the required number of copies.

Deleting portions of your molecule

CAChe provides two ways to delete selected workspace objects:

- cutting an object, placing it in the Windows Clipboard to paste into another file or Windows application
- deleting an object without placing a copy in the Windows Clipboard.

Cutting workspace objects

To cut a workspace object

1. Select the object that you want to cut by clicking on it with a selection tool.

   The object is highlighted to show that it is selected.

2. Do one of the following:

   - Choose **Edit** | **Cut**.
   - Press **Ctrl X**.
   - Select the toolbar button shown to the left.

   The selected object is copied to the Windows Clipboard and disappears from the workspace. The object remains in the Windows Clipboard until another selected object is copied or cut, or until you quit CAChe.

3. Do one of the following:

   - Choose **File** | **Open** to open a CAChe file if you want to paste the object from the Windows Clipboard into another CAChe file, or if the file is already open, activate it by clicking on its workspace.
   - If you want to paste the object into another Windows application, open or maximize the application, and open or activate the file into which you want to paste the cut object.

4. Do one of the following:
   - Choose **Edit** | **Paste**.
   - Press **Ctrl V**.
   - Select the toolbar button shown to the left (if you are pasting into a CAChe file).

   The cut object is pasted into the new document.
5. Continue to paste copies of the object until you have the required number of copies.

Deleting workspace objects

To delete workspace objects

1. Select the object that you want to delete by clicking on it with a selection tool.

   The object is highlighted to show that it is selected.
2. Do one of the following:
   - Choose **Edit** | **Delete**.
   - Press **Delete**.

   The selected object disappears from the workspace and is not copied to the Windows Clipboard.

The undo command

You can undo most editing actions performed on CAChe files. For example, if you delete part of your molecule by mistake, you can undo the delete action to retrieve the deleted object.

You can also reapply an editing action that you have undone by choosing the **Redo** menu option, as long as you have not performed another editing action since choosing **Undo**.

To undo an editing action

1. Choose **Edit** | **Undo**.

   Workspace objects resume their position or state prior to the last editing action that you performed on the workspace.

To redo an editing action after choosing undo

1. Choose **Edit** | **Redo**.

   Workspace objects resume their position or state after the last undo action you performed.

NOTE The **Undo** option from the **Edit** menu does not apply to the option **Edit** | **Save**, which you cannot undo.

Fusing ring structures

CAChe allows you to bond two ring structures together by fusing selected atoms from one ring onto selected atoms from the other ring. When fusing cyclic structures, you can either:

- fuse two atoms, where the first atom you select is replaced by the second atom you select. The second atom inherits all the connections of the first atom in addition to its own, and its valence is automatically adjusted.
- fuse two bonds, by fusing two sets of atoms. The first atom you select in the first set is replaced by the second atom in that set, and the first atom in the second set is replaced by the second atom in that set.

Once you fuse ring structures, use the **Beautify** menu to correct the bond lengths, geometry, and hybridization of the resulting structure.

To fuse two atoms

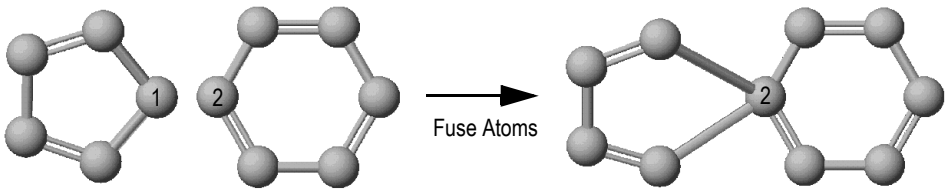
1. Select an atom in the first ring structure by clicking on it with the Select tool.

   The atom is highlighted to show that it is selected.

2. Hold down the **Shift** key and select the corresponding atom in the second ring structure by clicking on it with the Select tool.

   The atom is highlighted to show that it is selected.

   The following example shows the order of atom selection in the two rings, and the resulting structure when the second selected atom replaces the first. When you fuse atoms, the second atom you selected will replace the first atom you selected in the first ring structure.



3. Choose **Edit** | **Fuse Atoms**.

   The first atom you selected is replaced by the second atom you selected. The second atom becomes attached to all connecting bonds and atoms from the first atom.

4. Choose **Beautify** | **Comprehensive** to correct the valence, hybridization, ring structure, and molecular geometry of the resulting structure.

To fuse two bonds

1. Select an atom in the first ring structure by clicking on it with the Select tool.

   The atom is highlighted to show that it is selected.

2. Hold down the **Shift** key and select the corresponding atom in the second ring structure by clicking on it with the Select tool.

   The atom is highlighted to show that it is selected.

3. Choose **Edit** | **Fuse Atoms**.

   The first atom you selected is superimposed over the second atom you selected.

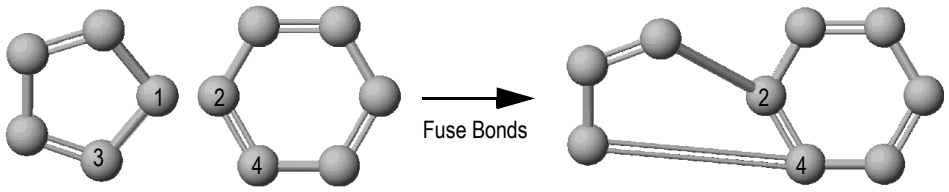
4. In the first ring structure, select the other atom connected to the bond you want to be superimposed by clicking on the atom with the Select tool.

   The atom is highlighted to show that it is selected.

5. Hold down the **Shift** key and select the corresponding atom in the second ring structure (i.e., the other atom connected to the bond you want to fuse) by clicking on it.

   The atom is highlighted to show that it is selected.

   The following example shows the order of atom selection in the two rings, and the resulting structure when the bond in the second ring structure replaces the first. When you fuse bonds, the bond in the second ring structure will replace the bond in the first ring structure.



6. Choose **Edit** | **Fuse Atoms**.

   The bond whose connecting atoms you selected in the first ring structure is replaced by the bond whose connecting atoms you selected in the second ring structure. The second bond inherits all the connecting bonds and atoms from the first bond.

7. Choose **Beautify** | **Comprehensive** to correct the valence, hybridization, ring structure, and molecular geometry of the resulting structure.

Grouping atoms

CACHe allows you to define and name a group of atoms, select a named atom group in the workspace, and then work with the group as a unit. You can also ungroup previously grouped atoms.

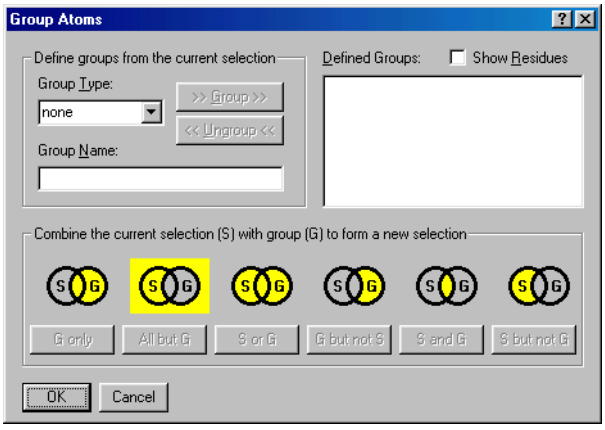
Defining a group

To form an atom group

1. Select the atoms that you want to participate in a group by clicking on them with a selection tool. If you are using the Select tool, hold down the **Shift** key when selecting more than one atom.

   The atoms are highlighted to show that they are selected.

2. Choose **Edit** | **Group Atoms** to display the Group Atoms dialog box.



3. Choose the **Group Type** from the pulldown. A group can be an active site, ligand, water, amino acid, nucleic acid, hetero type or none of these.
4. Click in the **Group Name** text box and type a name for the group of selected atoms.
5. Select **>>Group>>** to display the new group name in the **Defined Groups** list.

When you select a new or existing group in the **Defined Groups** list, the buttons in the section **Combine the current selection (S) with group (G) to form a new selection** are enabled.

Selecting groups and portions of groups

The Group Atoms dialog box refers to the atoms you selected in the workspace as **S**, and previously defined groups of atoms as **G**. Using set operator buttons in the dialog box, you can combine atoms from both **S** and **G** to:

- form new groups of atoms
- select portions of an existing group
- select portions of a current workspace selection.

Set diagrams in the Group Atoms dialog box illustrate the set operations, with the left circle representing the set **S** (selected atoms in the workspace), and the right circle representing the set **G** (a named atom group). The shaded region in each set diagram represents the workspace atoms that will be selected by the set operator.





The example set diagrams to the left represent the selection of all items belonging to a named atom group (far left) and the selection of everything but the atoms in a named group (left).

To select an existing group of atoms

1. Choose **Edit** | **Group Atoms** to display the Group Atoms dialog box.
2. Click on the group that you want to select in the **Defined Groups** list.
3. Select **G only**.
4. Select **OK** to close the Group Atoms dialog box.

   The atoms belonging to the chosen group are highlighted in the workspace to show that they are selected.

To select all workspace objects apart from an atom group

1. Choose **Edit** | **Group Atoms** to display the Group Atoms dialog box.
2. Select the group whose atoms you do not want to be selected in the workspace by clicking on the group in the **Defined Groups** list.
3. Select **All but G**.
4. Select **OK** to close the Group Atoms dialog box.

   Every workspace object is selected, apart from the atoms belonging to the group you chose in the Group Atoms dialog box. The atoms belonging to the chosen group are highlighted in the workspace to show that they are selected.

To select an existing group of atoms plus additional atoms

1. Select the additional atoms that you want to select by clicking on them with a selection tool.

   The atoms are highlighted to show that they are selected.
2. Choose **Edit** | **Group Atoms** to display the Group Atoms dialog box.
3. Select the group whose atoms you also want to select in the workspace by clicking on the group in the **Defined Groups** list.
4. Select **S or G**.
5. Select **OK** to close the Group Atoms dialog box.

   The atoms that you selected before opening the Group Atoms dialog box are still selected, and the atoms belonging to the chosen group in the Group Atoms dialog box are also selected in the workspace.

To select an existing group of atoms minus additional atoms

1. Select the grouped atoms that you do not want selected by clicking on them with a selection tool.

   The atoms are highlighted to show that they are selected.

2. Choose **Edit** | **Group Atoms** to display the Group Atoms dialog box.
3. Select the group that contains the atoms you selected in the workspace by clicking on the group in the **Defined Groups** list.
4. Select **G but not S**.
5. Select **OK** to close the Group Atoms dialog box.

   The atoms that you selected before opening the Group Atoms dialog box are no longer selected, while all other atoms belonging to the group chosen in the Group Atoms dialog box are selected in the workspace.

To select grouped atoms among selected workspace atoms

1. Select a number of atoms, or everything, in the workspace by clicking on the atoms or the workspace background with a selection tool.

   The selected atoms are highlighted.
2. Choose **Edit** | **Group Atoms** to display the Group Atoms dialog box.
3. Select the group that contains the atoms you want to remain selected in the workspace by clicking on the group in the **Defined Groups** list.
4. Select **S and G**.
5. Select **OK** to close the Group Atoms dialog box.

   Any atoms that were previously selected before opening the Group Atoms dialog box, and which belong to the group chosen in the Group Atoms dialog box, remain selected in the workspace.

To select non-grouped atoms among selected workspace atoms

1. Select a number of atoms, or everything, in the workspace by clicking on the atoms or the workspace background with a selection tool.

   The selected atoms are highlighted.

2. Choose **Edit** | **Group Atoms** to display the Group Atoms dialog box.
3. Select the group that contains the atoms you do not want selected in the workspace by clicking on the group in the **Defined Groups** list.
4. Select **S but not G**.
5. Select **OK** to close the Group Atoms dialog box.

   Any atoms that were previously selected before opening the Group Atoms dialog box, and which don't belong to the group chosen in the Group Atoms dialog box, remain selected in the workspace.

To ungroup a previously named group

1. Choose **Edit** | **Group Atoms** to display the Group Atoms dialog box.
2. Select the group that you want to ungroup by clicking on the group in the **Defined Groups** list.
3. Select **<<Ungroup<<**.
4. The group is no longer displayed in the **Defined Groups** list.
5. Select **OK** to close the Group Atoms dialog box.

   Any atoms belonging to that group still remain in your molecule, but the association between them is broken.

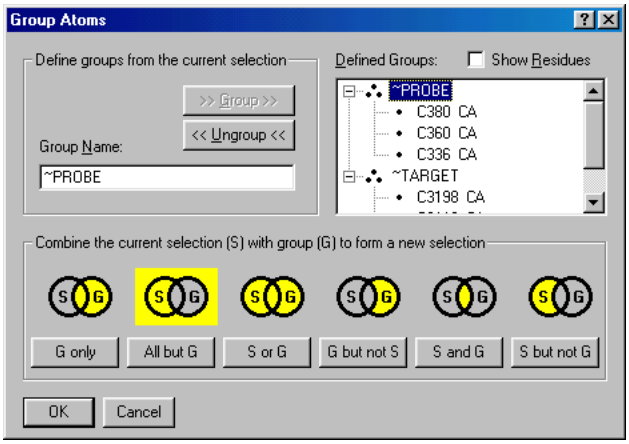
Changing atom order in groups

Atoms in atom groups have an order. Atom order is important when superimposing atom groups as explained in *"Superimposing with ordered atom groups"*, p 8-7.

To change atom order in an existing group of atoms

1. Choose **Edit** | **Group Atoms** to display the Group Atoms dialog box.
2. In the **Defined Groups** list, click on the plus symbol (+) next to the group that you want to reorder. The group expands to display

the name of each atom in the group.



3. Drag the atom names to place them in the required order.

   Atoms are placed after the atom they are dropped on. To move an atom to the top position in the list, drag it on top of the group name.

4. Select **OK** to close the Group Atoms dialog box.

   The atoms belonging to the chosen group are highlighted in the workspace to show that they are selected and the order of the atoms in the group has been changed.

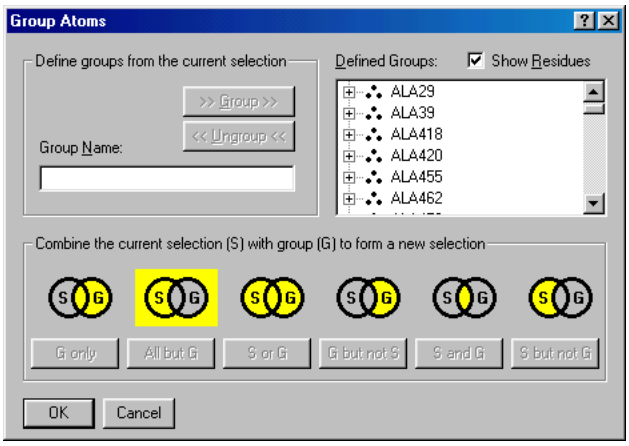
Showing residues in Group Atoms dialog box

Residues are special atom groups that are added automatically when biomolecules are imported from PDB files or built with the Sequence View window.

To view atom groups that are residues

1. Choose **Edit | Group Atoms** to display the Group Atoms dialog box. Check **Show | Residues** in the Group Atoms dialog box.

The list of residues appears in the Defined Groups list.



The order of atoms in a residue is important. You should not change the order of atoms in residues.

If you need to create an ordered group using all the atoms in a residue, select that residue and then create a new group with a different name (see *"Defining a group"*, p 7-24). The new group will not be classified as a residue and you can reorder the atoms in the new group.

8 Investigating Molecular Geometry

Overview

This chapter describes how to measure and adjust aspects of the geometry of your chemical sample, including how to:

- identify and invert any chiral centers in your chemical sample
- generate a mirror image of your molecule
- compare the molecular geometry of two structures
- measure atom distance and bond angle values using geometry labels
- lock geometry labels
- lock atoms
- disable locked geometry and repair broken locked geometry labels
- add search labels to create varying conformations of the structure.

Contents

Working with chiral centers **8-2**
Viewing chiral centers 8-2
Inverting chiral centers 8-3
Mirroring a molecule **8-5**
Superimposing molecules **8-6**
Superimposing by atoms 8-6
Superimposing with ordered atom groups 8-7
Calculating the RMS error 8-10
Specifying angles and distances **8-12**
Specifying atom distance 8-13
Specifying bond angle 8-14
Specifying dihedral angle 8-15
Specifying improper torsion angles 8-17
Working with geometry labels **8-19**
Defining geometry labels while viewing atom distance and bond length 8-19
Defining geometry labels from the Adjust menu 8-21
Changing geometry label appearance 8-21
Deleting geometry labels 8-26
Labeling H-Bonds 8-27
Labeling Bumps 8-28
Locking geometry labels **8-29**
Broken geometry locks 8-31
Locking atoms **8-32**
Hiding locked atom labels 8-33
Selecting locked atoms 8-34
Disabling locked geometry **8-35**
Working with search labels **8-37**
Specifying a new geometry label as a search label 8-37
Changing a geometry label to a search label 8-40
Defining search labels automatically 8-41
Manipulating search labels 8-43
Animating search labels 8-44

Working with chiral centers

CAChe includes helpful functions to make working with the chiral centers in your chemical sample easier. CAChe allows you to:

- identify chiral centers by labeling selected asymmetric carbons
- invert the bonded neighbors of a chiral carbon.

Viewing chiral centers

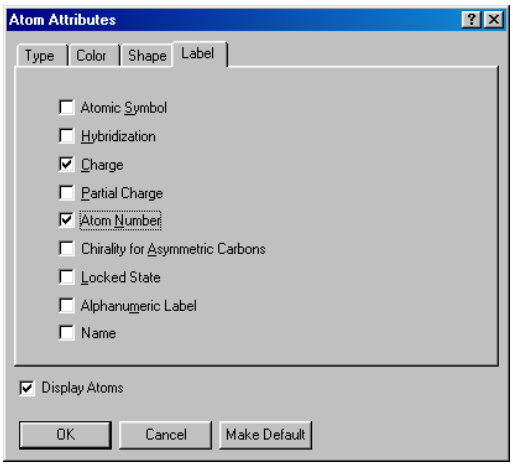
Label asymmetric tetrahedral carbons in the workspace with an **R** or an **S** to indicate the chirality. You can hide or display the labels you add to chiral carbons.

To label chiral centers

1. Select the carbon atoms or molecule for which you want to label chirality by clicking on the atoms or molecule with a selection tool.

   The atoms are highlighted in the workspace to show that they are selected.

2. Choose **View** | **Atom Attributes** to display the Atom Attributes dialog box.



3. Select the **Label** tab to display a list of atom labeling options.
4. Select the **Chirality for Asymmetric Carbons** check box so that it is enabled.
5. Select **OK** to close the Atom Attributes dialog box.

   All selected asymmetric tetrahedral carbon atoms are labeled with an **R** or an **S** to indicate the chiral center and the chirality. When drawing and modifying a structure, it is not uncommon that the four substituents and the central atom will be situated in, or close to, the plane. In this instance, CAChe may display an incorrect chiral assignment. The correct chiral assignment is displayed after the structure has been beautified, or optimized.

Inverting chiral centers

To invert the bonded neighbors of a chiral carbon, select a chiral center and swap two connecting bonds. The **R** and **S** labels that indicate chirality are also exchanged after you invert chirality.

There are two exceptions to the way CAChe swaps bonds while inverting chirality:

- if two bonds of the central atom are in a ring structure and two are not, the two that are not part of a ring become inverted.
- if the chiral center has three or more bonds in fused ring structures, you cannot invert chirality.

To invert chirality

1. Use a selection tool to select the carbon atom at the chiral center for which you want to invert chirality.

   The atoms are highlighted in the workspace.
2. Do one of the following:
   - Choose **Edit** | **Invert Chirality**.
   - Press **Ctrl I**.

   The two connecting bonds in the selected chiral center are swapped and the labels **R** and **S** are exchanged in the workspace.

📖 NOTE When you invert a chiral center with four neighboring atoms that are equally free to move, you can control which atoms are swapped by first locking the geometry of the two atoms you want to remain unchanged. Refer to *"Locking atoms"*, p 8-32, for details.

Mirroring a molecule

CAChe allows you to mirror the x, y, and z coordinates of selected atoms about the y and z plane through the center of the workspace. Mirroring a molecule is most useful for generating the enantiomer (mirror image) of a chemical sample.

To mirror a molecule

1. Select the atoms or molecule that you want to mirror by clicking on the atoms or molecule with a selection tool.

   The atoms are highlighted in the workspace to show that they are selected.

2. Choose **Edit** | **Mirror**.

   The selected atoms or molecule are mirrored about the y, z plane of the workspace.

NOTE CAChe cannot mirror a structure with locked atoms, or atoms that participate in locked geometry, if the mirroring involves breaking the locks. If you want to mirror such a molecule, disable the locks first.

Refer to *"Locking geometry labels"*, p 8-29, and *"Locking atoms"*, p 8-32, for details about disabling locks.

Superimposing molecules

Superimposing by atoms

You can compare the molecular geometry of two structures by superimposing one or more atoms in one structure on corresponding atoms in the other structure. You can select up to twenty-five pairs of atoms, one set of twenty-five atoms from each structure.

CAChe superimposes the selected atoms from both molecules to coincide with each other as much as possible. You can then compare any differences in structural geometry, indicated by the RMS value.

When selecting atoms from two different structures to superimpose on each other, you must select the atoms in a precise order. Use one of the following two selection methods:

- select the same number of atoms from both molecules in the same order. For example, if you want two atoms from each molecule to coincide, select two atoms from the first molecule and then select the corresponding two atoms from the second molecule.
- select one atom in the first molecule, and then select the corresponding atom in the second molecule, then select another atom in the first structure, and the corresponding atom in the second structure, until you have selected the number of atoms that you want to coincide.

📖 NOTE The structure that moves to accomplish the superimposition is the one that contains the first atom you select.

To superimpose two molecules

1. Select the atoms that you want to be superimposed on another structure's atoms by clicking on the atoms with the Select tool.
2. Do one of the following:
   - Select the same number of corresponding atoms in the second structure in exactly the same order that you selected the atoms in the first structure.

- Select one atom in the first molecule, and then select the corresponding atom in the second molecule, then select another atom in the first structure, and the corresponding atom in the second structure, until you select the required number of atoms.

3. Choose **Analyze** | **Superimpose**.

   The molecule that contains the first atom that you selected moves to overlap the other molecule. The selected atoms are highlighted to show that they are still selected. An RMS error is displayed which indicates the error in molecular geometry between the two structures.

4. Do one of the following to move the molecules apart again:
   - Choose **Edit** | **Undo**
   - Press **Ctrl Z**.
   - Select one molecule by clicking on it with the Select Molecule tool and click and drag to move the selected molecule to one side.

Superimposing with ordered atom groups

You can compare the molecular geometry of two structures by superimposing an ordered group in one structure on the corresponding ordered group in the other structure. The selected groups should be in different molecules, but the molecules can be in the same workspace or in different workspaces.

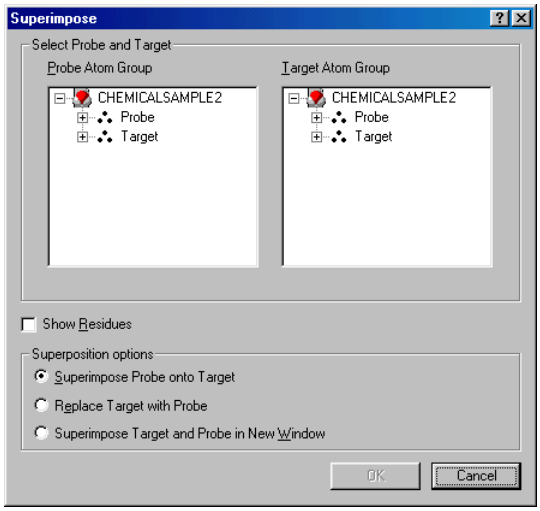
CAChe superimposes the atoms in the selected groups from both molecules so that they coincide with each other as much as possible. You can then compare any differences in structural geometry, indicated by the RMS value.

When superimposing atoms, the atoms are superimposed in the order that they are defined in the group.

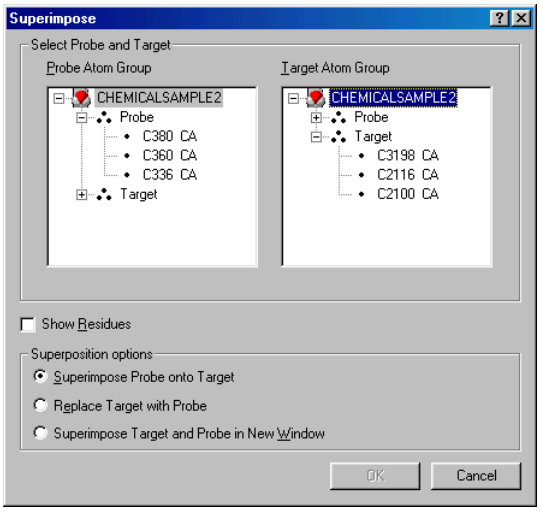
Before you can superimpose groups, you must define the groups as described in *"Defining a group"*, p 7-24.

To superimpose two molecules by atom group

1. Choose **Analyze | Superimpose Groups**. The Superimpose dialog appears.



2. Click the plus symbol (+) next to the groups name. The ordered list of atoms appears.



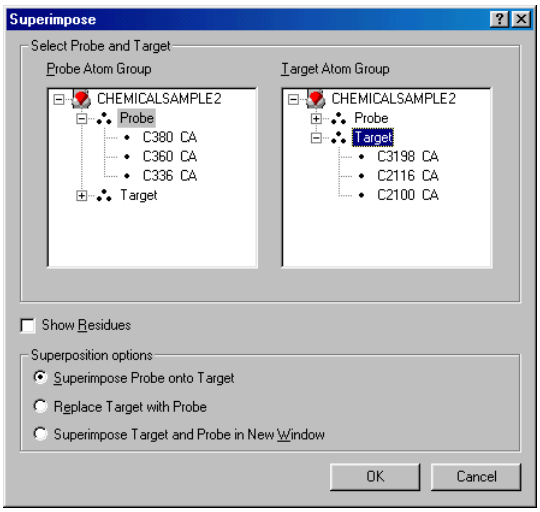
   Atoms in the probe are superimposed on atoms in the target in order.

3. If the order needs to be changed, drag the atoms so that each atom in the probe group corresponds in order to the atom you

want it superimposed on in the target group. Alternatively, drag the atoms in the target group.

The first atom in the probe group will be matched with the first atom in the target group for superposition and so forth until either all of the probe atoms are matched or all of the target atoms are matched. The number of atoms in the probe group and the target group can be different. Left over atoms at the end are not included in the superposition.

4. Select one group from each molecule.



5. Choose the **Superimpose Option** and press **OK**.

   The molecule that contains the probe group moves to overlap the target group in the other molecule. The selected atoms are highlighted to show that they are still selected. An RMS error is displayed which indicates the error in molecular geometry between the two structures.

6. Do one of the following to move the molecules apart again:

   - Choose **Edit** | **Undo**. There is no undo if molecules were superimposed in a new window.
   - Press **Ctrl Z**.
   - Select one molecule by clicking on it with the Select Molecule tool and click and drag to move the selected molecule to one side.

TIP To superimpose multiple molecules in a single window, repeatedly superimpose new probes against the target in the window where the first superposition takes place.

Calculating the RMS error

The RMS indicates the error in molecular geometry between two structures.

To calculate the RMS error

1. Select the atom(s) in the structure for which you want the RMS to be calculated.
2. Select the same number of corresponding atom(s) in the second structure in exactly the same order that you selected the atoms in the first structure.
3. Choose **Analyze | Calculate RMS Error**.

   The RMS error is displayed in the workspace.
4. To move the position of the RMS value, click in the centre of the value with the left mouse button, and drag to another part of the workspace.

To select the atoms involved in the RMS calculation

1. Position the Select Group tool over the RMS label, and select it using the left mouse button.

   The atoms involved in the calculation are selected.
2. Choose **Analyze | Superimpose**.

   The two molecules are superimposed.

To select the two molecules involved in the RMS calculation

1. Position the Select Group tool over the RMS label, and select it using the left mouse button.

   The two molecules that are involved in the calculation are

selected.

This enables you to distinguish the molecules involved in the RMS calculation from other molecules in the workspace.

Specifying angles and distances

CAChe allows you to measure and adjust distances and angles in a molecule, so that you can view and change the exact internal coordinates of a structure. You can also measure and adjust angle and distance values between atoms belonging to different molecules.

You can measure and change the following angles and distances:

- atom distance
- bond angle
- dihedral angle
- improper torsion.

When measuring angles and distances, the order in which you select the participating atoms is crucial to the resulting geometry adjustment. In all cases, the atom you select first is the atom that moves to achieve the new value of the angle or distance.

The values you can measure and adjust depend on the number of selected atoms:

- if two atoms are selected, you can measure and adjust atom distance
- if three atoms are selected, you can measure and adjust bond angles
- if four atoms are selected, you can measure and adjust dihedral angles and improper torsion.

You can also choose to label bond angles and atom distances in the workspace by applying geometry labels.



Refer to *"Working with geometry labels"*, p 8-19, for information on applying geometry labels.

Specifying atom distance

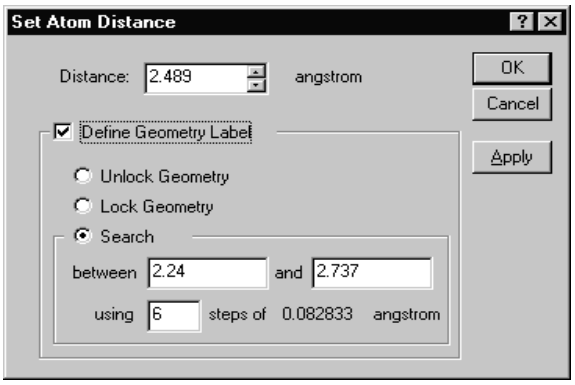
You can view and adjust the distance between two atoms in the same workspace.

To measure and adjust atom distance

1. Select the two atoms between which you want to measure atom distance by clicking on an atom with the Select tool, then holding down the **Shift** key and clicking on the second atom.

   If you are adjusting atom distance, ensure that the first atom you select is the atom that you want to move.

2. Choose **Adjust** | **Atom Distance** to display the Set Atom Distance dialog box.



   The current atom distance value in angstroms is displayed in the **Distance** text box.

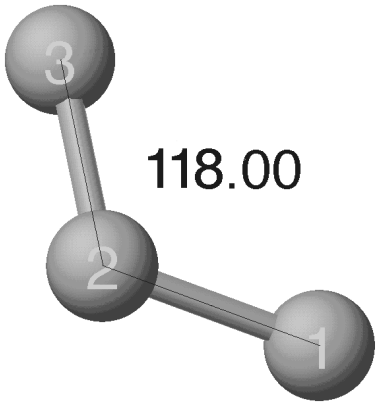
3. Do one of the following:
   - Click in the **Distance** text box and type the new atom distance value that you require.
   - Select the **Distance** text box arrow buttons to increase or decrease the current atom distance value to the value that you require.
4. Select **Apply** to view the results of the new atom distance value in the workspace.

The first atom that you selected moves to increase or decrease the atom distance to the value that you specified in the **Distance** text box.

5. Select **OK** to accept the new atom distance value and to close the Set Atom Distance dialog box.

Specifying bond angle

Measure and adjust the angle between two bonds by selecting the three participating atoms in the order in which the atoms span the angle, with the second atom positioned at the fulcrum of the angle. The following example shows a labeled bond angle, with the atoms labeled in the order of selection.



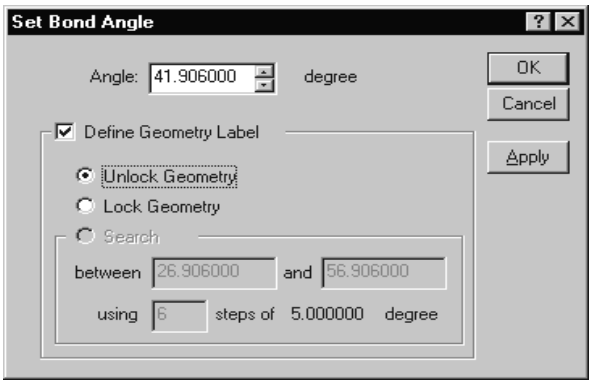
To measure and adjust bond angle

1. Select the three atoms between which you want to measure bond angle by clicking on the first atom with the Select tool, then holding down the **Shift** key and clicking on the second and third atom.

   If you are adjusting the bond angle, ensure that the first atom you select is the atom that you want to move.

2. Choose **Adjust** | **Bond Angle** to display the Set Bond Angle dialog box.

   The current bond angle value in degrees is displayed in the **Angle** text box.

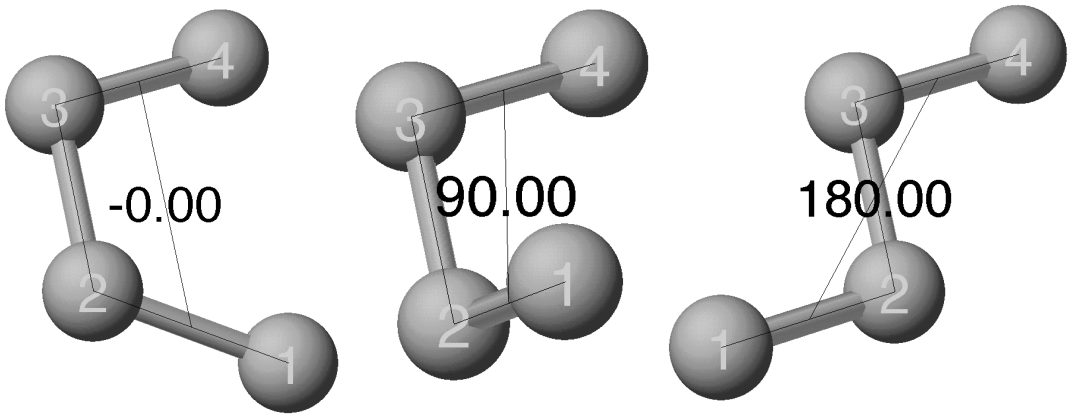


3. Do one of the following:
   - Click in the **Angle** text box and type the new bond angle value that you require.
   - Select the **Angle** text box arrow buttons to increase or decrease the current bond angle value to the value that you require.
4. Select **Apply** to view the results of the new bond angle value in the workspace.

   The first atom that you selected moves to increase or decrease the bond angle to the value that you specified in the **Angle** text box.
5. Select **OK** to accept the new bond angle value and close the Set Bond Angle dialog box.

Specifying dihedral angle

View a dihedral angle value by selecting four atoms and then measuring the rotational angle between the bond connecting the first and second atoms, and the bond connecting the third and fourth atoms. The following three examples show a dihedral angle, with the atoms labeled in the order of selection in each example.

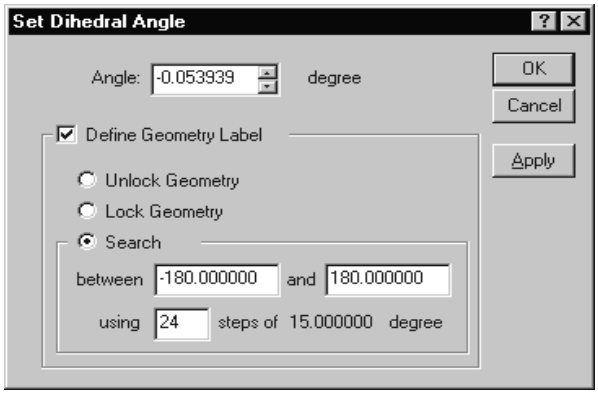


To measure and adjust dihedral angles

1. Select the four atoms that encompass the two bonds between which you want to measure the dihedral angle, by clicking on the first atom with the Select tool, then holding down the **Shift** key and clicking on the second, third and fourth atom.

   If you are adjusting the dihedral angle, ensure that the first atom you select is the atom that you want to move.

2. Choose **Adjust** | **Dihedral Angle** to display the Set Dihedral Angle dialog box.



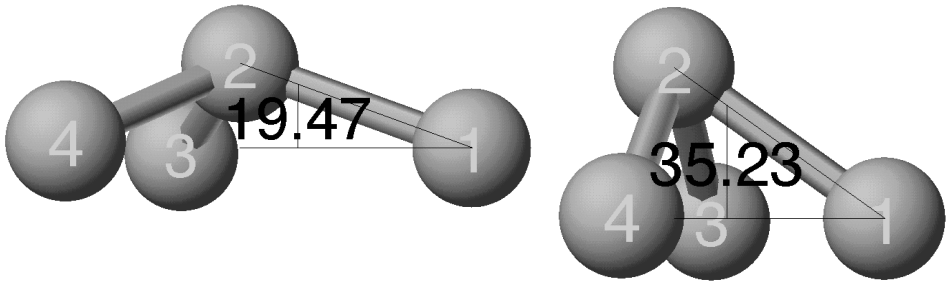
   The current dihedral angle value in degrees is displayed in the **Angle** text box.

3. Do one of the following:
   - Click in the **Angle** text box and type the new dihedral angle value that you require.
   - Select the **Angle** text box arrow buttons to increase or decrease the current dihedral angle value to the value that you require.
4. Select **Apply** to view the results of the new dihedral angle value in the workspace.

   The first atom that you selected moves to increase or decrease the dihedral angle to the value that you specified in the **Angle** text box.
5. Select **OK** to accept the new atom distance value and close the Set Dihedral Angle dialog box.

Specifying improper torsion angles

View an improper torsion angle by selecting four atoms and then measuring the angle between the bond connecting the first and second atoms, and the projection of that same bond on to the plane formed by the first, third and fourth atoms. The following two examples show improper torsion angles, with the atoms labeled in the order of selection in each example.

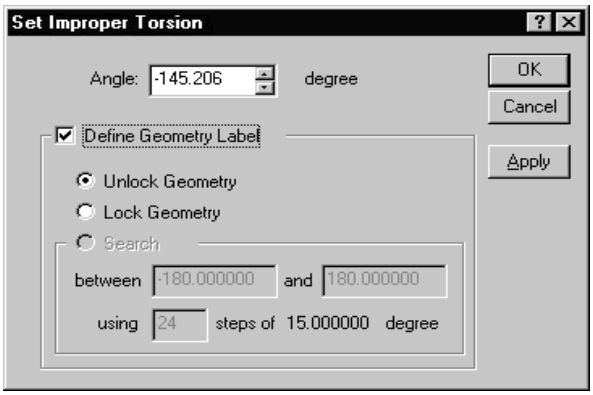


To measure and adjust improper torsion

1. Select the four atoms that form the improper torsion angle by clicking on the first atom with the Select tool, then holding down the **Shift** key and clicking on the second, third and fourth atom.

If you are adjusting the improper torsion angle, ensure that the first atom you select is the atom that you want to move.

2. Choose **Adjust | Improper Torsion** to display the Set Improper Torsion dialog box.



The current improper torsion value in degrees is displayed in the **Angle** text box.

3. Do one of the following:
   - Click in the **Angle** text box and type the new improper torsion value that you require.
   - Select the **Angle** text box arrow buttons to increase or decrease the current improper torsion value to the value that you require.
4. Select **Apply** to view the results of the new improper torsion angle value in the workspace.

   The first atom that you selected moves to increase or decrease the improper torsion angle to the value that you specified in the **Angle** text box.
5. Select **OK** to accept the new improper torsion value and close the Set Improper Torsion dialog box.

Working with geometry labels

Geometry labels identify the participating atoms and the current value of a specific angle or distance. Use geometry labels to:

- identify specific geometry attributes of your chemical sample
- display existing values of your chemical sample's internal coordinates
- lock atom distances and bond angles at their current values.

Refer to *"Locking geometry labels"*, p 8-29, for further details.

You can define geometry labels in three ways:

- when viewing and adjusting values for atom distance, bond angle, improper torsion, and dihedral angles
- directly from the **Adjust** menu
- automatically by generating dihedral angle search labels, a type of geometry label, using the CAChe Geometry Label Wizard.

Refer to *"Working with search labels"*, p 8-37, for information on creating and using search labels.

Defining geometry labels while viewing atom distance and bond length

Add a geometry label while viewing or adjusting an atom distance or bond length value.

To add a geometry label to a distance or angle

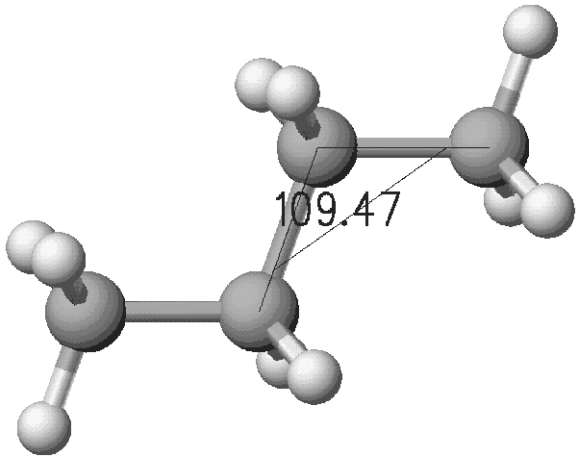
1. Select the required number of atoms for the distance or angle you want to label by clicking on the first atom with the Select tool, then holding down the **Shift** key and clicking on the remaining atoms.

For example, select two atoms if you want to label atom distance, three atoms if you want to label a bond angle, or four atoms if you want to label an improper torsion or dihedral angle.

2. Choose one of the following menu options:
   - **Adjust | Atom Distance**
   - **Adjust | Bond Angle**
   - **Adjust | Improper Torsion**
   - **Adjust | Dihedral Angle.**

   The Set Atom Distance, Set Bond Angle, Set Dihedral Angle, or Set Improper Torsion dialog box is displayed.
3. Select the **Define Geometry Label** check box so that it is enabled.
4. Select **Apply** to view the geometry label in the workspace.

   A geometry label identifies the participating atoms and displays the value of the distance or angle in the workspace. The following example shows a geometry label.



5. Select **OK** to accept the geometry label and close the Set Atom Distance, Set Bond Angle, Set Dihedral Angle, or Set Improper Torsion dialog box.

Defining geometry labels from the Adjust menu

If you do not need to adjust atom distance or bond angle values, you can also add geometry labels to your chemical sample directly from the **Adjust** menu, without displaying the Set Atom Distance, Set Bond Angle, or Set Dihedral Angle dialog box.

You cannot define an improper torsion geometry label in this way.

To define a geometry label directly from the Adjust menu

1. Select the required number of atoms for the distance or angle you want to label by clicking on the first atom with the Select tool, then holding down the **Shift** key and clicking on the remaining atoms.

   For example, select two atoms if you want to label atom distance, three atoms if you want to label a bond angle, or four atoms if you want to label a dihedral angle.

2. Do one of the following:
   - Choose **Adjust** | **Define Geometry Label**.
   - Press **Ctrl L**.

   A geometry label identifies the participating atoms and displays the value of the distance or angle in the workspace.

Changing geometry label appearance

Once you have added geometry labels to your chemical sample, you can also choose to:

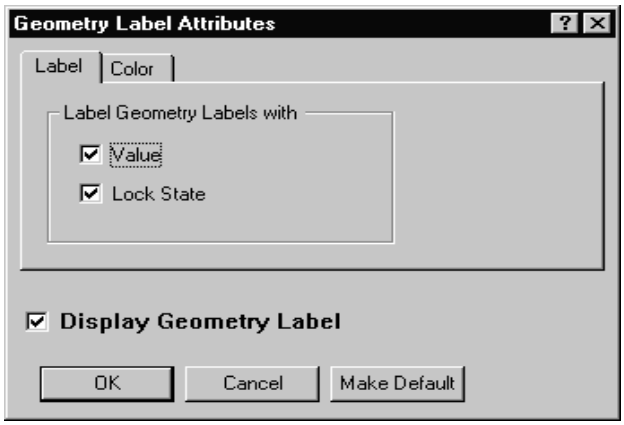
- hide or display geometry labels
- hide or display the value and locked state of a geometry label
- color geometry labels by label type or by the standard text color defined in the CAChe color palette.

Hiding geometry labels

Hide or display selected geometry labels in the workspace.

To hide geometry labels

1. Select the geometry label that you want to hide by clicking on the numeral portion of the label with the Select tool.
2. Choose **View** | **Geometry Label Attributes** to display the Geometry Label Attributes dialog box.



3. Select the **Display Geometry Labels** check box so that it is disabled.
4. Select **OK** to close the Geometry Label Attributes dialog box.

   The geometry label that you selected is no longer displayed in the workspace.

To redisplay geometry labels

1. Do one of the following to select everything in the workspace:
   - Click on an empty area of the workspace with a selection tool.
   - Choose **Edit** | **Select All**.
   - Press **Ctrl A**.
2. Choose **View** | **Geometry Label Attributes** to display the Geometry Label Attributes dialog box.

3. Select the **Display Geometry Labels** check box so that it is enabled.
4. Select **OK** to close the Geometry Label Attributes dialog box.

   All geometry labels in the workspace are displayed.

Hiding text in geometry labels

Hide and display the following text in a geometry label:

- the value of the distance or angle that the geometry label represents
- the locked state of the geometry label.



Refer to *"Locking geometry labels"*, p 8-29, for further details.

To hide the geometry label value

1. Select the geometry label whose value you want to hide by clicking on the numeral portion of the label with the Select tool.
2. Choose **View | Geometry Label Attributes** to display the Geometry Label Attributes dialog box.
3. Select the **Label** tab to display the **Label geometry labels with** panel.
4. Select the **Value** check box so that it is disabled.
5. Select **OK** to close the Geometry Label Attributes dialog box.

   The geometry label you selected no longer displays the value it represents.

To redisplay the geometry label value

1. Select the geometry label whose value you want to display by clicking on the label with the Select tool.
2. Choose **View | Geometry Label Attributes** to display the Geometry Label Attributes dialog box.
3. Select the **Label** tab to display the **Label geometry labels with** panel.

4. Select the **Value** check box so that it is enabled.
5. Select **OK** to close the Geometry Label Attributes dialog box.

   The geometry label you selected displays the value it represents.

To hide the locked state of a geometry label

1. Select the geometry label whose locked state you want to hide by clicking on the numeral portion of the label with the Select tool.
2. Choose **View** | **Geometry Label Attributes** to display the Geometry Label Attributes dialog box.
3. Select the **Label** tab to display the **Label geometry labels with** panel.
4. Select the **Lock State** check box so that it is disabled.
5. Select **OK** to close the Geometry Label Attributes dialog box.

   The geometry label you selected no longer displays an **L** if the geometry label is locked, or an **LB** if the geometry label is locked and the lock has been broken, or an **LD** if the geometry label lock is disabled.

To redisplay the locked state of a geometry label

1. Select the geometry label whose locked state you want to redisplay by clicking on the numeral portion of the label with the Select tool.
2. Choose **View** | **Geometry Label Attributes** to display the Geometry Label Attributes dialog box.
3. Select the **Label** tab to display the **Label geometry labels with** panel.
4. Select the **Lock State** check box so that it is enabled.
5. Select **OK** to close the Geometry Label Attributes dialog box.

   The geometry label you selected displays an **L** if the geometry label is locked, or an **LB** if the geometry label is locked and the lock has been broken, or an **LD** if the geometry label lock is disabled.

Refer to *"Locking geometry labels"*, p 8-29, for information on locked geometry labels and broken geometry label locks.

Refer to *"Disabling locked geometry"*, p 8-35, for information on disabling locks.

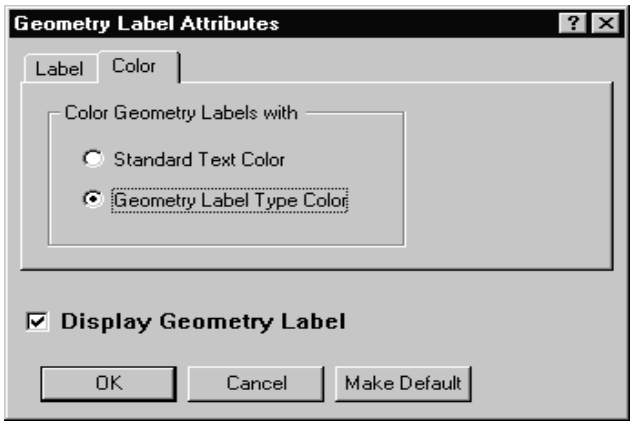
Changing geometry label color

Color geometry labels in one of two ways:

- by label type
- by the standard text color defined in the color palette.

To color geometry labels by label type

1. Select the geometry label whose color you want to change by clicking on the label with the Select tool.
2. Choose **View** | **Geometry Label Attributes** to display the Geometry Label Attributes dialog box.



3. Select the **Color** tab.
4. Select the **Geometry Label Type Color** radio button, in the Color Geometry Labels with section, to enable it.
5. Select **OK** to close the Geometry Label Attributes dialog box.

   The geometry label you selected is displayed in the color assigned to its geometry label type.

To color geometry labels by standard text color

1. Select the geometry label whose color you want to change by clicking on the numeral portion of the label with the Select tool.
2. Choose **View** | **Geometry Label Attributes** to display the Geometry Label Attributes dialog box.
3. Select the **Color** tab.
4. Select the **Standard Text Color** radio button, in the **Color Geometry Labels with** section, to enable it.
5. Select **OK** to close the Geometry Label Attributes dialog box.

   The geometry label you selected is displayed in the color assigned to standard text in the CAChe color palette.

Refer to *"Editing the color palette"*, p 6-38, for information on editing the CAChe color palette.

Deleting geometry labels

Delete a geometry label in one of two ways:

- using the **Delete** key
- using the **Adjust** menu options.

To delete a geometry label using the Delete key

1. Select the geometry label you want to delete by clicking on the label with the Select tool.
2. Press **Delete**.

To delete a geometry label using the Adjust menu

1. Select the geometry label you want to delete by clicking on the label with the Select tool.
2. Choose one of the following, depending on the distance or angle that the label is representing:
   - **Adjust** | **Atom Distance** to display the Set Atom Distance

dialog box.

- **Adjust | Bond Angle** to display the Set Bond Angle dialog box.
- **Adjust | Improper Torsion** to display the Set Improper Torsion dialog box.
- **Adjust | Dihedral Angle** to display the Set Dihedral Angle dialog box.

3. Select the **Define Geometry Label** check box so that it is disabled.
4. Select **OK** to close the Set Atom Distance, Set Bond Angle, Set Dihedral Angle, or Set Improper Torsion dialog box.

   The geometry label you selected is no longer displayed in the workspace.

Labeling H-Bonds

To label hydrogen bonds within a selection and between the selected atoms and the set of visible and unselected atoms do the following.

To label all hydrogen bonds

1. Select the atoms whose hydrogen bonds you wish to label with the Selection tool, the Select molecule tool or the Select Group tool.
2. Choose **Analyze | Label H-Bonds**.

   Blue hydrogen bond labels are created between any selected hydrogen-bonded atom and any visible atom it is hydrogen bonded to. In this analysis, hydrogen bonds are formed between any hydrogen atom attached to O, N, S or F and all O, N or S hydrogen acceptors that are within 2.2 Å.

   Because H-bond labeling is based on a distance criterion, H-bond labels may appear in unexpected locations if your structure is poorly refined.

Labeling Bumps

To label unselected atoms that are too close to the selected atoms do the following.

To label all bumps

1. Select the atoms that you wish to analyze for bumps with the Selection tool, the Select molecule tool or the Select Group tool.
2. Choose **Analyze | Label Bumps**.

   Orange bump labels are created between any selected atom and any visible, unselected atom that is within 0.87 times the sum of their van der Waals radii and that is not bonded or in the same bond angle.

   Because bump labeling is based on a distance criterion, labels may appear in unexpected locations if your structure is poorly refined. A large number of bump labels can indicate a structure requiring further refinement.

Locking geometry labels

Locking geometry labels allows you to freeze an atom distance, bond angle, dihedral angle, or improper torsion angle at a specified value, ensuring that the locked portions of your chemical sample do not change during an experiment.

Lock geometry labels in one of two ways:

- lock a label while defining the geometry label using the Set Atom Distance, Set Bond Angle, or Set Improper Torsion dialog box
- lock an existing geometry label directly from the **Adjust** menu.

To lock a geometry label while defining it

1. Select the required number of atoms for the distance or angle you want to label by clicking on the first atom with the Select tool, then holding down the **Shift** key and clicking on the remaining atoms.

   For example, select two atoms if you want to create and lock a label for an atom distance, three atoms if you want to create and lock a label for a bond angle, or four atoms if you want to create and lock a label for an improper torsion or dihedral angle.

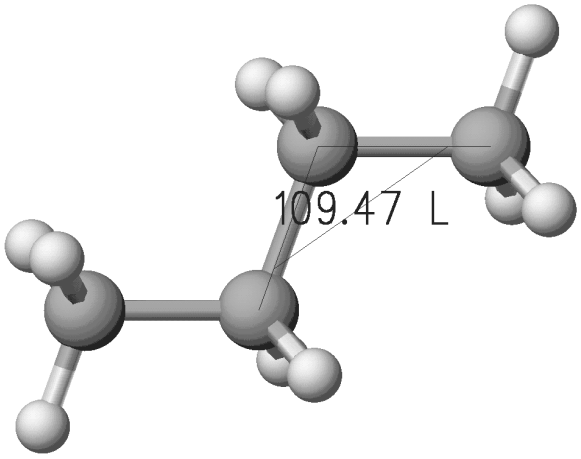
2. Choose one of the following menu options:
   - **Adjust | Atom Distance**
   - **Adjust | Bond Angle**
   - **Adjust | Improper Torsion**
   - **Adjust | Dihedral Angle.**

   The Set Atom Distance, Set Bond Angle, Set Dihedral Angle, or Set Improper Torsion dialog box is displayed.

3. Select the **Define Geometry Label** check box so that it is enabled.
4. Select the **Lock Geometry** radio button so that it is enabled.

5. Select **OK** to close the Set Atom Distance, Set Bond Angle, Set Dihedral Angle, or Set Improper Torsion dialog box.

   A geometry label displays the value of the distance or angle in the workspace and an **L** to indicate that the label is locked. The following example shows a locked geometry label.



To lock an existing geometry label

1. Select the geometry label you want to lock by clicking on the numeral portion of the label with the Select tool.
2. Choose **Adjust | Lock**.

   The geometry label displays the value of the distance or angle in the workspace and an **L** to indicate that the label is locked.

To unlock a geometry label

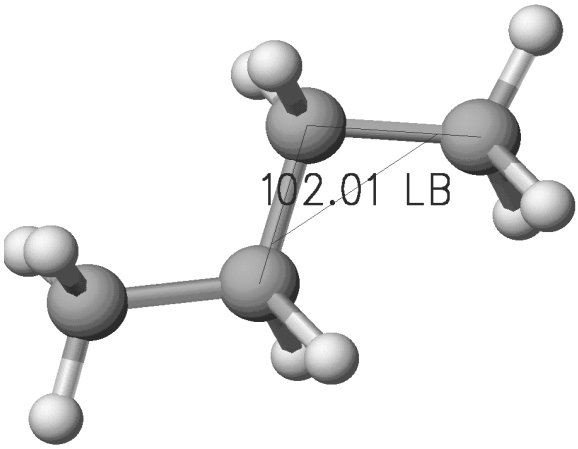
1. Select the locked geometry label by clicking on the numeral portion of the label with the Select tool.
2. Choose **Adjust | Unlock**.

   The geometry label no longer displays an **L**.

Broken geometry locks

Locks change to broken locks if the geometry of the locked structure changes. Changes can occur while you are editing your chemical sample with locks disabled. Running some experiments using the computational applications Mechanics, ZINDO, or MOPAC can also result in slightly altered values for locked coordinates.

Broken locks are labeled with **LB** in the workspace to indicate that a broken lock is present. The following example shows a broken geometry label lock.



Repairing broken locks

If the coordinates of a locked geometry label change, you can return the value of a broken geometry label lock to its locked value.

To repair a broken geometry label lock

1. Select the geometry label with a broken lock by clicking on the numeral portion of the label with the Select tool.
2. Choose **Adjust | Repair Locked Geometry Labels**.

   The spatial relationship that the geometry label represents returns to the locked value.

Locking atoms

You can freeze the location of an atom by locking its x, y, and z coordinates in the workspace.

When you perform an experiment on a chemical sample with locked atoms, locks are enforced even if the lock is currently disabled. Locking atoms is useful to:

- perform calculations that require some atoms to remain at a fixed position, while others are free to move.

  For example, you could lock the structural bulk of an enzyme to optimize the surface of an enzyme and its substrate. To study the effect of a zeolite cage on the deformation of a molecule that passes through it, you could lock the atoms in the zeolite and optimize the molecule in various positions in the zeolite.

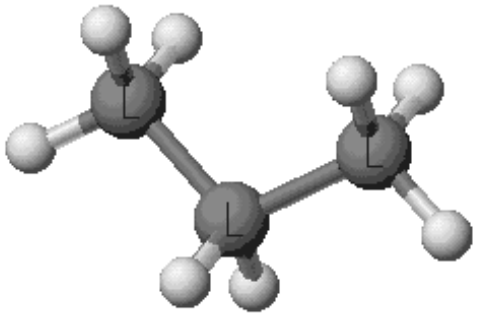
- fix the location of an atom that might move out of the workspace area when you scale and rotate several structures at once.

You can also unlock atoms at any time.

To lock an atom

1. Select the atoms you want to lock using a selection tool.
2. Choose **Adjust | Lock.**

   The atoms are locked at their current x, y, z workspace coordinates and are labeled with an **L**. The following example shows labeled locked atoms.



To unlock atoms

1. Select the atoms you want to lock by clicking on the atoms with a selection tool.
2. Choose **Adjust | Unlock.**

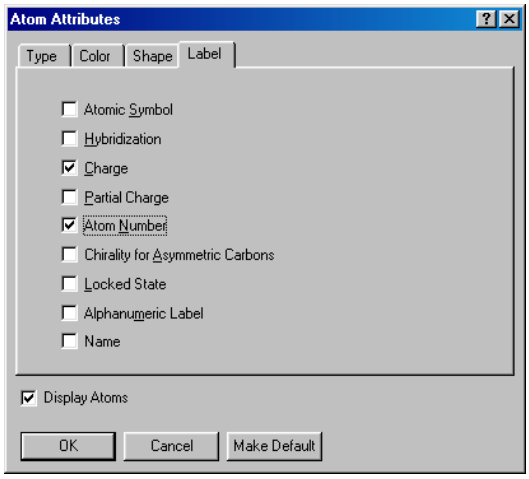
   The selected atoms are unlocked and the **L** label is no longer displayed.

Hiding locked atom labels

You can show or hide the **L** label which indicates a locked atom.

To hide locked atom labels

1. Select the locked atoms whose label you want to hide by clicking on the atoms with a selection tool.
2. Choose **View | Atom Attributes** to display the Atom Attributes dialog box.



3. Select the **Label** tab to display a list of options for labeling atoms.
4. Select the **Locked State** check box so that it is disabled.
5. Select **OK** to close the Atom Attributes dialog box.

   The selected locked atoms no longer display the **L** label.

To redisplay locked atom labels

1. Select the locked atoms whose label you want to redisplay by clicking on the atoms with a selection tool.
2. Choose **View** | **Atom Attributes** to display the Atom Attributes dialog box.
3. Select the **Label** tab to display a list of options for labeling atoms.
4. Select the **Locked State** check box so that it is enabled.
5. Select **OK** to close the Atom Attributes dialog box.

   The selected locked atoms display an **L** label to indicate that they are locked.

Selecting locked atoms

You can select all the locked atoms in the workspace, whether or not the atoms are labeled as locked.

To select all locked atoms

1. Choose **Edit** | **Select Locked Atoms.**

   All locked atoms in the workspace are highlighted to show that they are selected.

Disabling locked geometry

You can enable or disable locked geometry at any time. Locks are enabled by default until you disable them. CAChe allows you to disable:

- locked geometry labels
- locked atoms.

Disabling the locks on geometry labels and atoms allows you to move the participating atoms around the workspace. However, if you do not return the participating atoms of a locked geometry label to their locked values, you create a broken lock which is displayed when you enable locked geometry again.

Refer to *"Broken geometry locks"*, p 8-31, for information on repairing broken geometry label locks.

Moving a locked atom while locks are disabled just moves the locked atom to a new location. When locks are enabled again, the atom is displayed as locked in the new location.

When you begin a CAChe experiment, disabled geometry label locks and atom locks are automatically enabled and used by the computational applications to freeze the locked coordinates of the participating atoms.

To disable locked geometry

1. Choose **Adjust | Enable Locks.**

   The check mark next to the **Enable Locks** drop-down list option is no longer displayed, indicating that this option is disabled. Locked geometry labels and atoms display an **LD** label to indicate that there are disabled locks present.

To enable locked geometry

1. Choose **Adjust | Enable Locks.**

   A check mark is displayed next to the **Enable Locks** drop-down list option, indicating that this option is enabled.

   Locked geometry labels which have not been broken and locked atoms display an **L** to indicate that they are locked. Broken locked geometry labels display an **LB** to indicate that a broken lock is present.

Working with search labels

Search labels are a form of geometry label that vary the value of the atom distance or bond angle represented by the geometry label. Search labels are used in CAChe experiments to define a range of conformations for a molecule while computing the energy of each conformation.

When creating a search label, you specify a range of values for an atom distance, bond angle, improper torsion, or dihedral angle. During the CAChe experiment, the labeled distance or angle is moved through the range of search label values to create a number of conformations for the molecule, so that the energy of each conformation can be measured.

For example, you can vary a dihedral angle through 360 degrees, stopping every 15 degrees to compute the energy of the molecule at those conformations.



Refer to Chapter 13, *"Optimization and Energy Calculations"*, and Chapter 14, *"Investigating Low-energy Conformations"*, for information on how CAChe experiments use search labels.

You can define search labels in three ways:

- specify a new geometry label as a search label while creating the geometry label
- modify an existing geometry label to become a search label
- use the Geometry Label Wizard to create one or more search labels automatically.

Specifying a new geometry label as a search label

You can define a search label for an atom distance, bond angle, dihedral angle, or improper torsion angle while creating a new geometry label.

To create a search label while defining a geometry label

1. Select the required number of atoms for the distance or angle you want to label by clicking on the first atom with the Select tool, then holding down the **Shift** key and clicking on the remaining atoms.

   For example, select two atoms if you want to create a search label for an atom distance, three atoms if you want to create a search label for a bond angle, or four atoms if you want to create a search label for an improper torsion or dihedral angle.

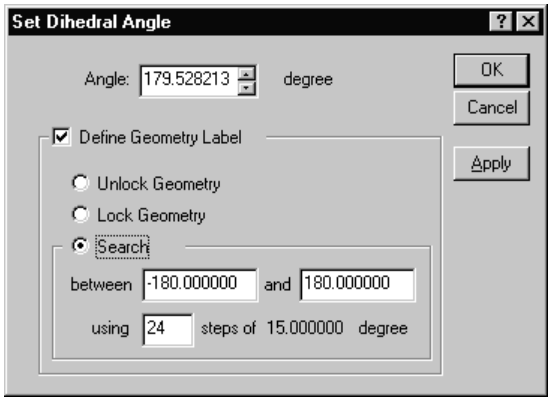
2. Choose one of the following menu options:
   - **Adjust | Atom Distance**
   - **Adjust | Bond Angle**
   - **Adjust | Improper Torsion**
   - **Adjust | Dihedral Angle.**

   The Set Atom Distance, Set Bond Angle, Set Dihedral Angle, or Set Improper Torsion dialog box is displayed.

3. Select the **Define Geometry Label** check box so that it is enabled.

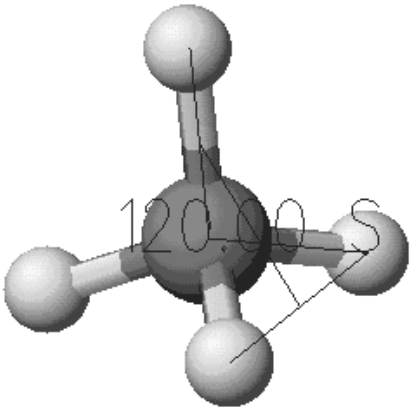
4. Select the **Search** radio button so that it is enabled.

   A range of default values and steps between those values are displayed in the text boxes beneath the **Search** radio button.



5. If you want to change the default values, do one or all of the following:
   - Click in the **between** text box and enter a new value for the start of the value range.
   - Click in the **and** text box and enter a new value for the completion of the value range.
   - Click in the **using** text box and enter a new value for the number of steps throughout which you want the range of values to be varied.
6. Select **OK** to close the Set Atom Distance, Set Bond Angle, Set Dihedral Angle, or Set Improper Torsion dialog box, and to define the search label with the specified value range and number of steps.

   A search label displays the value of the distance or angle in the workspace and an **S** to indicate that the label is a search label. The following example shows a search label.



Changing a geometry label to a search label

You can modify an existing geometry label to change it into a search label.

To change a geometry label into a search label

1. Select the geometry label by clicking on the numeral portion of the label with the Select tool.

   The geometry label is highlighted to show that it is selected.

2. Choose the relevant menu option for the selected geometry label type from one of the following:

   - **Adjust | Atom Distance**
   - **Adjust | Bond Angle**
   - **Adjust | Improper Torsion**
   - **Adjust | Dihedral Angle**

   The Set Atom Distance, Set Bond Angle, Set Dihedral Angle, or Set Improper Torsion dialog box is displayed.

3. Select the **Search** radio button so that it is enabled.

   A range of default values and steps between those values are displayed in the text boxes beneath the **Search** radio button.

4. If you want to change the default values, do one or all of the following:

   - Click in the **between** text box and enter a new value for the start of the value range.
   - Click in the **and** text box and enter a new value for the completion of the value range.
   - Click in the **using** text box and enter a new value for the number of steps throughout which you want the range of values to be varied.

5. Select **OK** to close the relevant dialog box, and to define the search label with the specified value range and number of steps.

   A search label displays the value of the distance or angle in the workspace and an **S** to indicate that the label is a search label.

Defining search labels automatically

You can use the CAChe Geometry Label Wizard to automatically generate dihedral angle search labels for selected bonds in your molecule.

When defining labels, the Geometry Label Wizard excludes the following:

- ring structures
- locations that conflict with locked geometry labels
- locked atom coordinates
- any other search labels already present in your sample.

In addition, you can specify the following to be excluded from the automatic generation of dihedral angle search labels:

- one or more bond types
- terminal groups such as CH_3, CCl_3, NH_2, or OH.

NOTE Before you generate automatic search labels, you might want to lock the coordinates of an atom near the center of the molecule, to prevent the sample from moving to the far edges of the workspace during the generation of the varying conformations.



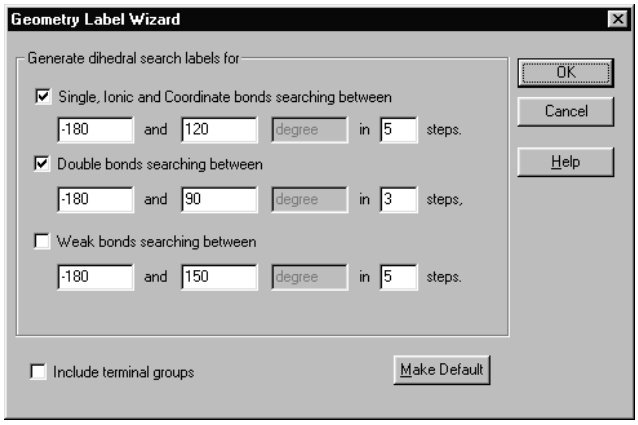
Refer to *"Locking atoms"*, p 8-32, for details about locking the workspace coordinates of atoms.



To define dihedral search labels using the Geometry Label Wizard

1. Do one of the following:
   - Select the whole molecule by clicking on it with the Select Molecule tool.
   - Select the bonds for which you want to generate search labels by clicking on one bond with the Select tool, holding down the **Shift** key, and clicking on the rest of the bonds.

2. Choose **Adjust | Geometry Label Wizard** to display the Geometry Label Wizard dialog box.



3. To include single, ionic, and coordinate bonds in the search label generation, select the **Single, Ionic and Coordinate bonds searching between** check box so that the radio button is enabled.

   A range of default values and steps between those values are displayed in the text boxes beneath the **Single, Ionic and Coordinate bonds searching between** check box.

4. If you want to change the default values, click in the relevant text box and type a new value for the start or end of the value range, or for the number of steps throughout the range.

5. To include double bonds in the search label generation, select the **Double bonds searching between** check box so that the radio button is enabled.

   A range of default values and steps between those values are displayed in the text boxes beneath the **Double bonds searching between** check box.

6. If you want to change the default values, click in the relevant text box and type a new value for the start or end of the value range, or for the number of steps throughout the range.

7. To include weak bonds in the search label generation, select the **Weak bonds searching between** check box so that it is enabled.

A range of default values and steps between those values are displayed in the text boxes beneath the **Weak bonds searching between** check box.

8. If you want to change the default values, click in the relevant text box and type a new value for the start or end of the value range, or for the number of steps throughout the range.
9. To include terminal groups, select the **Include terminal groups** check box so that it is enabled.
10. Select **OK** to generate dihedral angle search labels automatically, and to close the Geometry Label Wizard dialog box.

    Search labels display the value of the selected dihedral angles in the workspace and an **S** to indicate that the labels are search labels.

Manipulating search labels

You can manipulate search labels in exactly the same way as geometry labels using the following actions:

- selecting search labels by clicking on the numeral portion of the search label in the workspace
- changing the appearance of search labels by choosing **View | Geometry Label Attributes** to display labeling and coloring options
- modifying search labels and their values by choosing **Atom Distance**, **Bond Angle**, **Improper Torsion** or **Dihedral Angle** from the **Adjust** menu and editing search label values in the Set Atom Distance, Set Bond Angle, Set Dihedral Angle, or Set Improper Torsion dialog box.
- deleting search labels using the **Delete** key.



Refer to *"Working with geometry labels"*, p 8-19, for more information on performing the above actions on geometry labels.

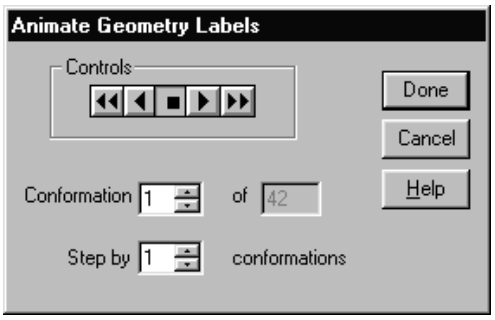
Animating search labels

You can animate your molecule so that it steps through every conformation created by the search labels you added to it. You can:

- animate the molecule from the first to the last conformation in the range
- animate the molecule from the last to the first conformation in the range
- stop at any individual conformation
- view the conformations step by step, or in a range of steps.

To animate search labels

1. Select the search labels that you want to animate in one of the following ways:
   - Select a molecule and its search label by clicking in the workspace background using a selection tool.
   - Select individual search labels by clicking on one label with the Select tool, holding down the **Shift** key, and clicking on the other search labels that you want to animate.
2. Choose **Adjust** | **Animate Geometry Labels** to display the Animate Geometry Labels dialog box.





3. Select the forward button, shown to the left, to animate your molecule from the first to the last conformation.

   The molecule in the workspace moves through each search label value in turn to create a range of conformations. The **Conformation** text box displays the position of the current

conformation in the range of conformations. The box to the right of the **Conformation** text box displays the total number of conformations in the range.



4. To stop the animation at a particular conformation, select the stop button, shown to the left.

   The molecule stops moving, and the **Conformation** text box displays the position of the current conformation in the range of conformations.



5. To animate your molecule from the last to the first conformation, select the reverse button, shown to the left.
6. To display a particular conformation in the range, do one of the following:
   - Select the up or down arrow buttons in the **Conformation** text box to increase or decrease the value displayed.
   - Click in the **Conformation** text box and enter the step number of the conformation you want to view.



7. To view the first conformation in the range, select the rewind button, shown to the left.

   The molecule moves to the first conformation in the range.



8. To view the last conformation in the range, select the forward button, shown to the left.

   The molecule moves to the last conformation in the range.

9. To modify the range of steps by which you are animating the molecule, do one of the following:
   - Select the up or down arrow buttons in the **Step by** text box to increase or decrease the value displayed.
   - Click in the **Step by** text box and type the number of steps by which you want to animate the molecule.
10. To finish the animation, do one of the following:
    - Select **Done** to close the Animate Geometry Labels dialog box and to display the conformation at which you finished the animation in the workspace.
    - Select **Cancel** to close the Animate Geometry Labels dialog box and to display the conformation before the animation.

9 Manipulating Biomolecules

Overview

This chapter describes how to open Protein Data Bank (PDB) files, view protein structures and sequences and build proteins and peptides from their sequence. You'll learn how to:

- open and view PDB molecules
- build peptides and proteins by sequence; mutate residues
- display secondary structure
- color sequences and structure by property
- compare and align sequences in separate proteins
- superimpose structures from sequences
- map protein and active site surfaces

Contents

Viewing biomolecules **9-2**
Saving a PDB molecule 9-6
Displaying proteins 9-6
Viewing PDB atom names 9-7
Highlighting residues 9-8
Coloring residues 9-8
Highlighting and displaying the backbone 9-9
Displaying the backbone N-C-C trace 9-10
Displaying ribbons 9-10
Displaying surfaces 9-11
Working in the Sequence View window **9-18**
Viewing sequence residues 9-18
The toolbar 9-19
The Sequence View window 9-20
The style bar 9-21
The tool palette 9-23
Changing the sequence style 9-25
Computing and viewing secondary structure 9-26
Numbering sequences 9-27
Coloring sequences by properties 9-28
Wrapping and hiding sequences 9-29
Changing biomolecules **9-31**
Mutating residues 9-31
Inserting residues 9-32
Deleting residues 9-33
Joining chains 9-33
Copying and pasting sequences 9-34
Building peptides and proteins 9-34
Building by homology 9-35
Changing secondary structure 9-37
Comparing biomolecules **9-39**
Aligning sequences 9-39
Matching selections 9-40
Select conserved 9-41
Superimposing biomolecules 9-42
Removing superposition 9-44
Extending the amino acid repository **9-45**
Nonstandard amino acid in a PDB file 9-45
Creating and adding a nonstandard amino acid with the Workspace 9-47

Viewing biomolecules

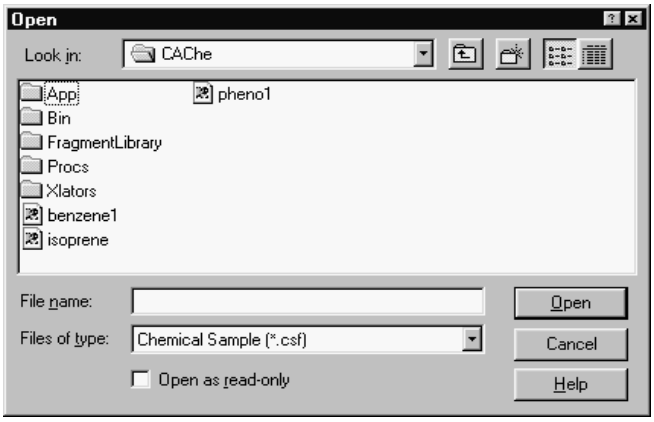
To view biomolecules contained in CAChe chemical sample files, simply open them as you would any other molecule.

In addition to viewing biomolecules that are contained in chemical sample files, CAChe can view biomolecules from structural databases like the Protein Data Bank maintained by the Research Collaboratory for Structural Bioinformatics (RCSB).

The structures of proteins and other biomolecules can be downloaded from `http://www.rcsb.org/pdb/` as PDB files. PDB files have an extension of `.pdb` or `.ent`. To view the 3D structure contained in a PDB file, you simply open it in the CAChe workspace.

To open a PDB file

1. Choose **File** | **Open** to display the Open dialog box.



2. Select the arrow button in the **Look in** drop down box to display a drop-down list of:
   - folders in the directory structure above the currently open folder
   - available drives from which you can open the file.
3. Choose the folder or drive where the file is located from the drop-down list.

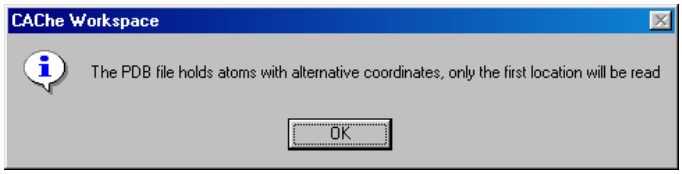


Do one of the following:

- To move up a level of folders to locate the folder containing the file, select the dialog box button shown to the left.
- To locate the file in a subfolder, click and drag the scroll bar in the scrolling list to display the folder where the file is located, and double-click on the folder to open it.

4. Select the arrow button in the **Files of type** box and choose **PDB (*.pdb, *.ent)** from the drop-down list.
5. Do one of the following:
   - Click and drag the scroll bar in the scrolling list to locate the file that you want to open, and select the file by clicking on it.
   - Click in the **File name** text box and type the file name of the file that you want to open.
6. Select **Open** to open the file and to close the Open dialog box.

NOTE If the PDB file contains alternative coordinates for atoms, you will see the dialog below and the first coordinates will be used.

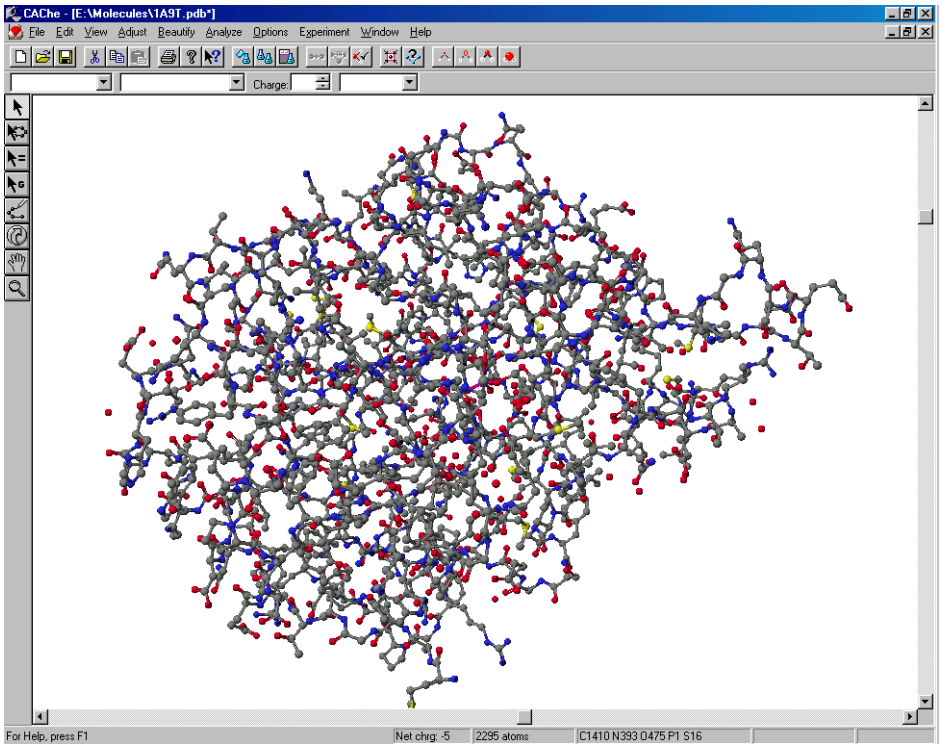


If you need to load the alternative coordinates, you must modify the PDB file using a text editor to make the alternative first before loading the file into CAChe.

CAChe uses a `het_dictionaryCIF.txt` file that resides in the CAChe directory to assign bonding and charges in HET groups. This file changes with each new update to the PDB. You should download the new version of this file from the PDB with each new release of the PDB to ensure that your HET group definitions are up-to-date.

If the PDB file contains HETATM records, you should use the Sequence View to select the HET residues and you should check them to see that the bond types and atom valencies are as expected for that structure.

A new workspace opens and the structure displays.

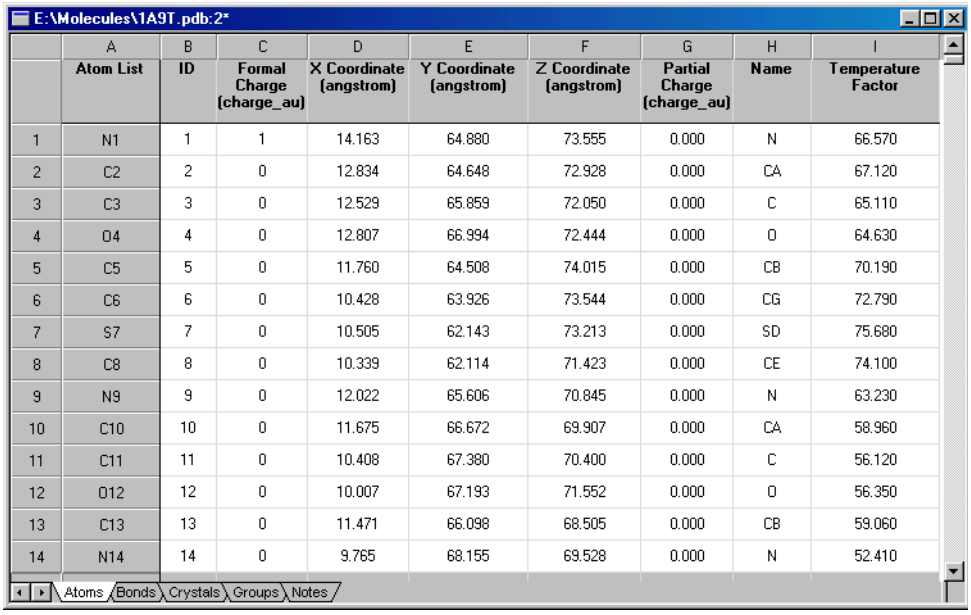


NOTE It may take a few seconds to load the PDB file, depending on its size or the number of atoms it contains.

At this point you should save the file as chemical sample with the appropriate name.

All of the information in the PDB file has been stored in the CACHe chemical sample format. For example, residues have been stored as Groups and you can use the Select Group tool to select residues.

To view this information, choose **Analyze | Chemical Properties Spreadsheet.** The chemical sample properties window appears.



E:\Molecules\1A9T.pdb:2*

	A Atom List	B ID	C Formal Charge (charge_au)	D X Coordinate (angstrom)	E Y Coordinate (angstrom)	F Z Coordinate (angstrom)	G Partial Charge (charge_au)	H Name	I Temperature Factor
1	N1	1	1	14.163	64.880	73.555	0.000	N	66.570
2	C2	2	0	12.834	64.648	72.928	0.000	CA	67.120
3	C3	3	0	12.529	65.859	72.050	0.000	C	65.110
4	O4	4	0	12.807	66.994	72.444	0.000	O	64.630
5	C5	5	0	11.760	64.508	74.015	0.000	CB	70.190
6	C6	6	0	10.428	63.926	73.544	0.000	CG	72.790
7	S7	7	0	10.505	62.143	73.213	0.000	SD	75.680
8	C8	8	0	10.339	62.114	71.423	0.000	CE	74.100
9	N9	9	0	12.022	65.606	70.845	0.000	N	63.230
10	C10	10	0	11.675	66.672	69.907	0.000	CA	58.960
11	C11	11	0	10.408	67.380	70.400	0.000	C	56.120
12	O12	12	0	10.007	67.193	71.552	0.000	O	56.350
13	C13	13	0	11.471	66.098	68.505	0.000	CB	59.060
14	N14	14	0	9.765	68.155	69.528	0.000	N	52.410

Atoms | Bonds | Crystals | Groups | Notes

Note that the sample properties for a PDB molecule contain several worksheets:

- **Atoms** contains atoms and their properties
- **Bonds** contains bonds and their properties
- **Groups** contains residues and their properties
- **Electrons** worksheet keeps track of nonbonded electron pairs so that the valence can be checked. Electrons are added when you beautify a structure and do not appear when the PDB file is first opened.
- **Notes** contains PDB REMARK, NOTE, SOURCE, COMPND and HEADER records information.

When a PDB file is opened in CAChe, some new information is automatically calculated and added. However, the information required for molecular modeling must still be added for example hydrogen atoms and atom hybridization.

To prepare a PDB molecule for molecular modeling

1. Choose **Edit | Select All**.
2. Choose **Beautify | Valence**

   Hydrogen atoms and electrons are added. If atoms do not have hybridization or electrons, then hybridization and electrons are added.

Only the geometry of hydrogen atoms and the hybridization and electrons around atoms that do not have hybridization already assigned are changed with these commands.

Saving a PDB molecule

As you work with this chemical sample, you may add additional information that you want to save.

To save a PDB molecule

1. Select **File | Save**.

When you save this workspace, you can chose to save it as a chemical sample file (`*.csf`), a PDB file, or other file type. Save the workspace as a chemical sample file (`*.csf`) to preserve all of the information you have added. Otherwise, information such as rendering style and computed atom properties will be lost.

Displaying proteins

You can display 3D structures from PDB files using the display options described in Chapter 6.

Refer to Chapter 6, *"Viewing Chemical Samples"* for details about display options for chemical samples.

In addition, you can:

- view PDB atom names
- highlight residues
- color the protein by residue property
- display the protein backbone

- view the protein as a ribbon.

Viewing PDB atom names

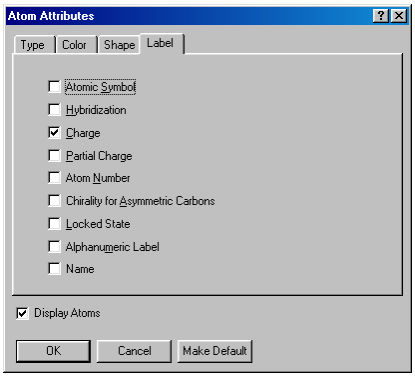
You can view atom names in the workspace.

To view the PDB atom names

1. Select the atoms or molecule for which you want to view the PDB names by clicking on the atoms, groups or molecule with the appropriate selection tool.

   The atoms are highlighted in the workspace to show that they are selected.

2. Choose **View** | **Atom Attributes** to display the Atom Attributes dialog box.



3. Select the **Label** tab to display a list of atom labeling options.
4. Select the **Name** check box so that it is enabled.
5. Select **OK** to display the PDB labels and close the Atom Attributes dialog box.

   Selected atoms are displayed with atom names. In large structures, atom names may be so small that they are not visible. Magnify the protein to see the atom names.

Highlighting residues



To highlight a residue

1. Choose the Select Group tool.

   Residues are special types of atom groups.

2. Select an atom in a residue.

   All the atoms that share a group with this atom are selected. Residues are identified by their PDB names.

To deselect a group

1. Position the Select Group tool over the selected group you want to deselect.
2. Press the shift key and the **left** mouse button to deselect the group.

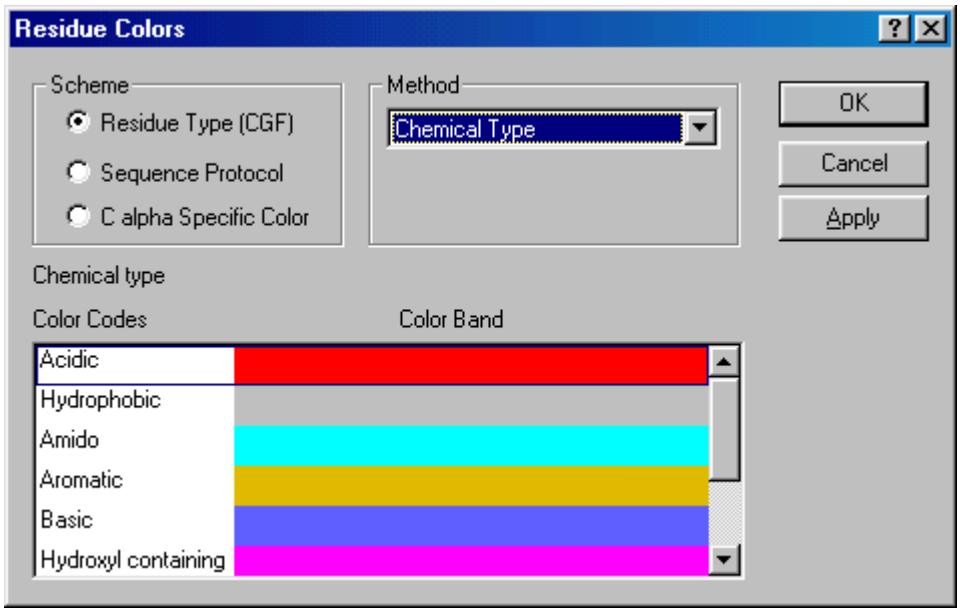
   The group is grayed out to show that it is deselected.

You can also use the Sequence View window to quickly select residues. See *"The selection tools"*, p 9-24 for details.

Coloring residues

To color all residues by the same scheme

1. Choose **View | Color by Residue**



The Residue Colors dialog opens.

2. Select the **Scheme** and **Method**.
3. Choose **OK**.

   The colors of all atoms in an amino acid residue are assigned based on the **Scheme** and **Method** selected. The change in color applies to selected, unselected, visible and hidden atoms.

To learn about the coloring schemes and methods, see *"Coloring sequences by properties"*, p 9-28 for details.

Highlighting and displaying the backbone

To highlight a backbone

1. Choose **Edit | Select Backbone**.

   All atoms that are marked as backbone atoms are selected and highlighted. All other atoms connected to the backbone are deselected.

To display a backbone only

1. Choose **Edit | Select Backbone**.

   All atoms that are marked as backbone atoms are selected and highlighted. All other atoms connected to the backbone are deselected.

2. Choose **View | Hide Unselected**.

   Atoms not in the backbone are hidden, and only the backbone is displayed.

Displaying the backbone N-C-C trace

To display the N-C-C protein backbone

1. Choose **View | Backbone N-C-C Trace**.

   The N-C-C atoms in each residue are selected and all other atoms connected to the backbone are deselected and hidden.

To redisplay all atoms

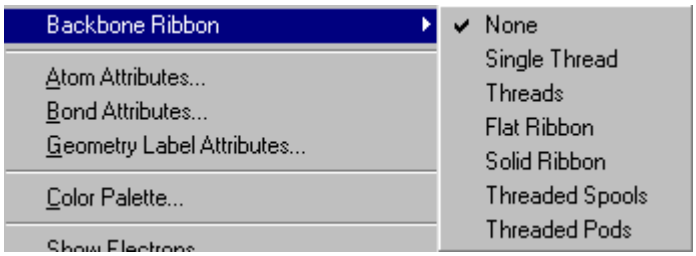
1. Choose **View | Show All**.

   All objects are displayed.

Displaying ribbons

To display the protein backbone as a ribbon

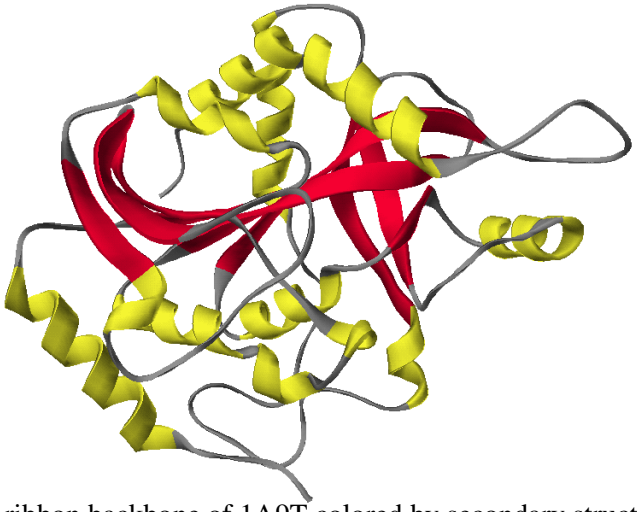
1. Choose **View | Backbone Ribbon**.



2. Choose the style: Single Thread, Threads, Flat Ribbon, Solid

Ribbon, Threaded Spools, Threaded Pods.

A splined ribbon in the chosen style and using the color set with **View | Residue Colors** is drawn.[1] The cubic B-spline follows the N-C-C atoms in each residue. All amino acid residues connected to the backbone are deselected and hidden. Nucleic acids, HET groups and waters remain visible.



Solid ribbon backbone of 1A9T colored by secondary structure

To redisplay all atoms

1. Choose **View | Backbone Ribbon | None**.

   All objects are displayed.

Displaying surfaces

With CAChe, you can display the accessible surface of

1. a protein accessible to a probe sphere of 1.4Å radius colored by hydrophobicity and hydrophilicity;
2. an active site adjacent pocket colored by the hydrophobic and hydrophilic properties required in a ligand for good binding;
3. a protein colored by the depth of the crevices in the surface.

1. Carson, M., *J. of Mol. Graphics*, **1985**, *5*, 103-106.

To display the protein accessible surface

1. With the Select Molecule Tool in the 3D Structure Window, select the protein.

NOTE The protein must have hydrogen atoms added first.

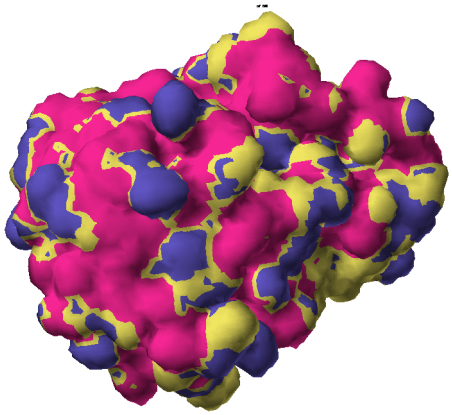
The protein highlights and all other objects dim.

2. Choose **View | Hide Unselected**.

The protein remains visible, all other objects disappear.

3. Choose **Analyze | Accessible surface**.

After a few seconds, a progress dialog appears and then the surface is drawn on the protein. The surface that is drawn is one



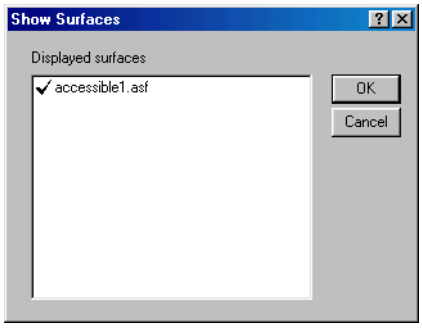
that would be accessible to, or touched by, a 1.4Å sphere rolling over the protein. Since water is approximately 1.4Å in size, this surface is sometimes called the solvent accessible surface.

The mauve (red) areas indicate regions of the protein surface where there are hydrogen bond acceptors (e.g. >C=O) within 3.0Å. The blue areas map regions of the protein where there are hydrogen bond donors (e.g. -OH or $-NH_2$) more than 3.0Å from a carbonyl oxygen and less than 2.6Å from a hetero hydrogen (-XH). The rest of the surface is colored cream and that indicates hydrophobic regions of the protein.

To hide the protein accessible surface

1. Choose **Analyze | Show Surfaces**.

   The Show Surfaces dialog appears.



2. Uncheck the `.asf` surface and choose **OK**.

   The dialog closes and the surface disappears.

To delete the protein accessible surface

1. With the protein accessible surface displayed, click on the **asf** surface label.

   Both the surface label and the surface highlight, all other objects dim.

2. Choose **Edit | Delete**.

   The surface and its label disappear from the screen and are removed from the chemical sample file. However, the surface `.asf` files remain in the `.iso` folder. You delete `.asf` files with the Windows Explorer after they have been deleted from the chemical sample.

To display the crevice surface

1. With the Select Molecule Tool in the 3D Structure Window, select the protein.

NOTE The protein must have hydrogen atoms added first.

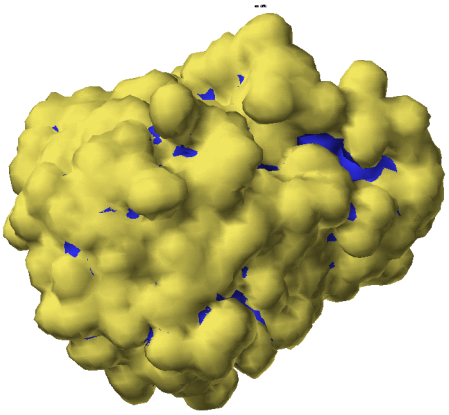
   The protein highlights and all other objects dim.

2. Choose **View | Hide Unselected**.

   The protein remains visible, all other objects disappear.

3. Choose **Analyze | Crevice surface**.

   After a few seconds, a progress dialog appears and then the surface is drawn on the protein. The surface that is drawn is one



   that would be accessible to, or touched by, a 1.4Å sphere rolling over the protein. Since water is approximately 1.4Å in size, this surface is sometimes called the solvent accessible surface.

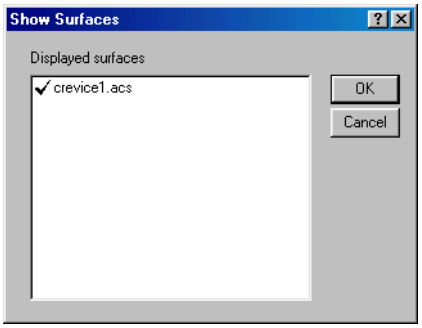
   The blue areas map deep crevices in the protein surface. The depth is measured from an outer, smoother surface accessible to a 2.9Å sphere. Blue areas are points farther than 3.0Å from the outer surface. The cream areas map areas that are within 3.0Å of the outer surface.

   Relatively large, deep and complex-shaped canyons are potential binding sites for ligands.

To hide the crevice surface

1. Choose **Analyze | Show Surfaces**.

The Show Surfaces dialog appears.



2. Uncheck the `.acs` surface and choose **OK**.

   The dialog closes and the surface disappears.

To delete the protein crevice surface

1. With the protein crevice surface displayed, click on the **acs** surface label.

   Both the surface label and the surface highlight, all other objects dim.

2. Choose **Edit | Delete**.

   The surface and its label disappear from the screen and are removed from the chemical sample file. However, the surface `.acs` files remain in the `.iso` folder. You delete `.acs` files with the Windows Explorer after they have been deleted from the chemical sample.

To display the ligand adjacent surface

1. With the Select Molecule Tool in the 3D Structure Window containing a ligand bound in a protein active site, select the ligand.

NOTE The protein and ligand must have hydrogen atoms added first.

   The ligand highlights and all other objects dim.

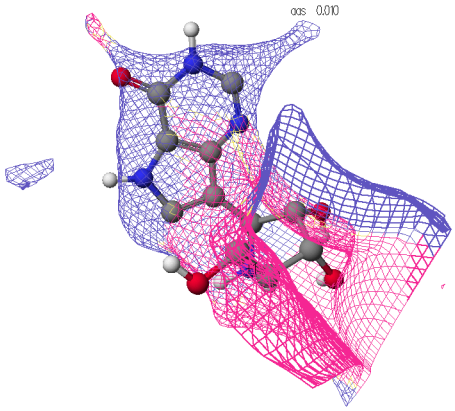
2. Choose **Analyze | Adjacent Surface - Pocket**.

   After a few seconds, a progress dialog appears and then the

surface of the protein adjacent to the ligand.

3. Choose **View | Hide Unselected**.

   The ligand and the surface remain visible. All other objects disappear.



The surface[1] that is drawn is one that is accessible to, or touched by, a 1.4Å sphere rolling over that portion of the protein adjacent to the ligand. This is the surface of the protein that interacts with the ligand and forms the pocket in which the ligand is docked.

The colors of the pocket indicate properties of an ideal ligand. The mauve (red) areas indicate regions of the protein surface where hydrogen bond acceptors (e.g. >C=O) are needed in the ligand for optimal binding. The blue areas map regions of the protein where nearby hydrogen bond donors (e.g. -OH or $-NH_2$) are needed for optimal binding in the ligand. The cream areas indicate where the ligand should have hydrophobic groups (e.g. $>CH_2$).

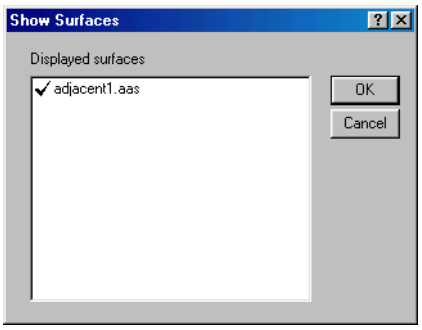
You can use this wire pocket to design new ligands with improved binding affinity by (1) filling empty space in the pocket with functional groups that bind to the protein and (2) trimming protruding groups. As a guide, carbonyl oxygens (>C=O) should touch the red mesh, hydrogens that hydrogen bond to the protein should stick through the blue mesh, and hydrophilic groups should be inside and away from the mesh.

1. Bohacek, R. and McMartin, C., *J Med Chem* **1992**, *35*, 1671-1684.

To hide the adjacent surface - pocket

1. Choose **Analyze | Show Surfaces**.

   The Show Surfaces dialog appears.



2. Uncheck the `.aas` surface and choose **OK**.

   The dialog closes and the surface disappears.

To delete the protein adjacent surface - pocket

1. With the protein adjacent surface displayed, click on the **aas** surface label.

   Both the surface label and the surface highlight, all other objects dim.

2. Choose **Edit | Delete**.

   The surface and its label disappear from the screen and are removed from the chemical sample file. However, the surface `.aas` files remain in the `.iso` folder. You delete `.aas` files with the Windows Explorer after they have been deleted from the chemical sample.

Working in the Sequence View window

The sequence data for a protein 3D structure that is open in CAChe is displayed in the Sequence View window. When you open multiple proteins, their sequence data are added to the Sequence View window. Only one Sequence View window can be open at one time. You use the sequence window to:

- view the sequence
- color the sequence by property
- mutate residues
- edit the sequence
- build peptides and proteins from residues
- analyze secondary structure
- adjust the conformation or secondary structure of a protein
- align sequences
- match selections and select conserved residues
- superimpose sequences.

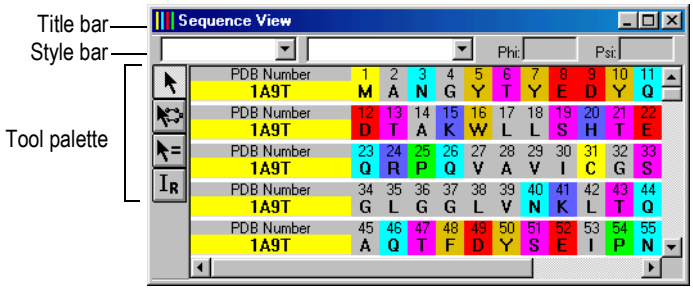
NOTE The Sequence View is available only with CAChe WorkSystem Pro, BioCAChe or BioMedCAChe.

Viewing sequence residues

To view a sequence

1. From a workspace window, choose **Analyze | Sequence** to display the sequence window. The Sequence View window displays sequences in rows that begin with the chemical sample

name.



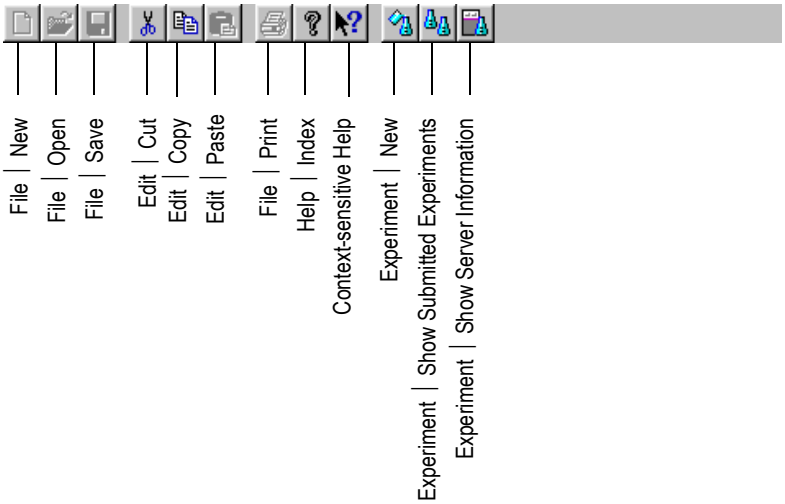
The sequence has a direction, starting from the N terminus of the first residue to the C terminus of the last one. Hetero groups are always displayed, but water molecules (HOH) are never displayed.

When you view a sequence, the Sequence View window comes to the front and the menus and toolbar change.

The toolbar

The Sequence View toolbar contains a collection of buttons that provide a shortcut to some of the menu options.

The following diagram shows the toolbar and the corresponding menu options that each button performs when the Sequence View window is at the front.



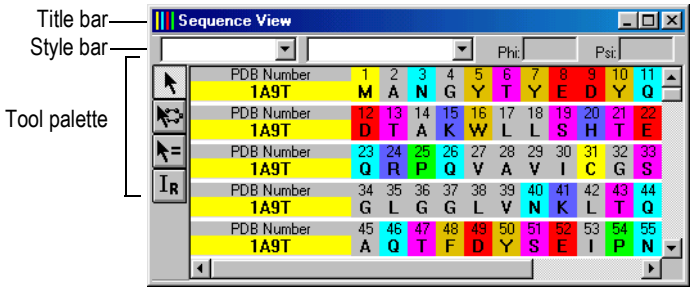
The Sequence View window

Although you can have many workspaces open at any time, there can be only one Sequence View window open at a time.

Any menu bar or toolbar commands you choose affect the active document window. To activate the Sequence View, click on it.

The main components of the Sequence View are:

- a title bar that displays the name of the document
- a Style bar with drop-down lists that enable you to change the residue type, secondary structure type, and Phi and Psi angles of selected parts of your protein
- a Tool palette that provides selection tools and a residue editing tool.



The Sequence View window

Residues for each chemical sample are shown using 1-letter or 3-letter codes on a line that wraps at the window boundary. An asterisk called the “chain terminal” marks the end of each protein chain. The at symbol ‘@’ marks the terminus of a cyclic peptide. Note that the chain terminal is not part of the structure and you cannot select the chain terminal.

Refer to *“Changing the sequence style”*, p 9-25 for details about changing display options for sequences such as 1- and 3-letter codes.

The Sequence View, the workspace and the Sample Property Windows work together. That is, selections or changes you make in one window are immediately reflected in the other two windows.

Residues shown as half intensity color are not selected. On displays with only 256 colors, residues that are not selected are gray. Residues highlighted in bright full intensity colors have one or more atoms or bonds selected. Residues with every atom selected are highlighted and surrounded by a black box.

Items copied in the Sequence View, the 3D Structure window or a Sample Properties view can be pasted into another view. Thus you can select a sequence in the Sequence View, then switch to the 3D Structure window to paste the residue sequence and adjust its position in 3D space.

The style bar

The Sequence View style bar provides three items that enable you to change or create features of selected parts of your molecule:

- residue type
- secondary structure type
- Phi and Psi angles.



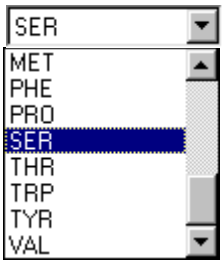
Example style bar

Use the style bar in conjunction with the workspace selection and inserting tools to:

- display the residue type and Phi-Psi angles of a selected residue
- mutate a residue from one type to another
- change Phi and Psi angles
- set a motif.

The Residue Type box

The Residue Type drop-down box lists the twenty standard amino acids.



Once you choose a residue from the Residue Type drop-down box, you can:

- insert a residue of that type
- mutate a selected residue to the type you select.

The Secondary Structure box

The Secondary Structure box provides a drop-down list of secondary structures that you can apply to:

- the next residue you insert
- a selected residue.



The Phi and Psi boxes

The Phi and Psi boxes are text boxes that you can use to enter values for the attachment angles for the residue.



Once you have selected or entered angles, you can:

- insert a residue with the specified Phi and Psi values
- change the Phi or Psi values of a selected residue.

Hiding the style bar

You can display or hide the sequence style bar.

To hide the sequence style bar

1. When the style bar is visible, choose **Options** | **Show Ribbon**.

   The style bar is no longer displayed at the top of the workspace.

   The check mark next to the **Show Ribbon** drop-down item on the Options menu no longer appears, indicating that the style bar is currently hidden.

To redisplay the sequence style bar

1. When the style bar is hidden, choose **Options** | **Show Ribbon**.

   The style bar is displayed at the top of the workspace.

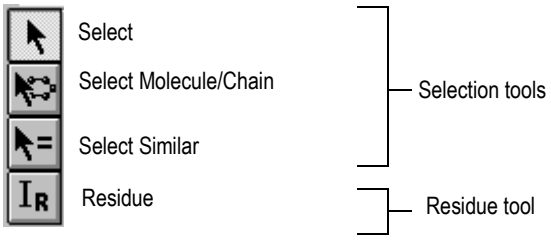
   A check mark appears next to the **Show Ribbon** drop-down item on the Options menu, indicating that the style bar is currently visible.

The tool palette

The sequence tool palette provides two types of tools:

- selection tools

- a residue tool for inserting residues



The selection tools

The tool palette contains the following selection tools:

- the Select tool (default), which selects individual residues or sequences
- the Select Molecule tool, which selects an entire molecule or sequence chain in a protein
- the Select Similar tool, which selects all residues of a similar type.

Choose a tool by clicking on it in the tool palette. When you choose a tool, the mouse cursor in the workspace changes shape to indicate which tool is currently selected.

The table below displays the selection tools as they appear in the tool palette, and their corresponding cursors:

Selection tool	Tool palette icon	Mouse cursor
• the Select tool (default)		
• the Select Molecule/ Chain tool		
• the Select Similar tool		

The Residue tool

Use the residue tool to edit residue sequences in the sequence window.

Editing Tool	Tool palette icon	Mouse cursor
• the Residue tool		

With the residue tool, you may type residues in a sequence. You must specify secondary structure type, and Phi and Psi angles first before typing a residue.

Changing the sequence style

To view 3-letter codes

1. Choose **View | 3-letter Code** to display 3-letter codes for all sequences.

   The 3-letter Code menu item is checked.

To view 1-letter codes

1. Choose **View | 1-letter Code** to display 1-letter codes for all sequences.

   The 1-letter Code menu item is checked.

The codes for the residues are listed in the table.

Residue	1-letter	3-letter code
Alanine	A	ALA
Arginine	R	ARG
Asparagine	N	ASN
Aspartic acid	D	ASP
Cysteine	C	CYS
Glutamine	Q	GLN
Glutamic acid	E	GLU
Glycine	G	GLY
Histidine	H	HIS
Isoleucine	I	ILE
Leucine	L	LEU
Lysine	K	LYS
Methionine	M	MET
Phenylalanine	F	PHE
Proline	P	PRO
Serine	S	SER
Threonine	T	THR
Tryptophan	W	TRP
Tyrosine	Y	TYR
Valine	V	VAL

Computing and viewing secondary structure

To view secondary structure

1. Choose **View | Secondary Structure** to display icons below each residue that show the secondary structure that is contained

in the PDB file.

The secondary structure is displayed in 1-letter codes defined in *"Defining secondary structure"*, p 21-4. If you delete, replace or insert residues, you change the secondary structure, and you must update the secondary structure information.

To compute secondary structure

1. Choose **Edit | Analyze Secondary Structure** to compute the secondary structure and display icons below each residue that show the secondary structure.

   The secondary structure is computed by the PDB standard Kabsch and Sander algorithm (see *"Defining secondary structure"*, p 21-4).

Numbering sequences

You can number sequences by the number assigned to residues within the original PDB file or from one to *n* using a ruler.

To number sequences

1. Do one of the following
   - **View | Residue numbers | PDB** to display the PDB number above each residue.

     The number displayed is the number obtained from the PDB file. Sequences do not necessarily start numbering from one and residues may have the same PDB number, but differ in PDB insertion code. The PDB numbers always define the order in the sequence.
   - **View | Residue numbers | Ruler** to display the sequence ruler above each residue.

     Sequence rulers always start from 1 and end with the number of the chain termini in the sequence. The ruler counts residues, gaps and chain termini.

During editing, the PDB number assigned to a residue may no longer reflect its position in the sequence. For example, editing the residue with PDB number 10 might appear after the residue with PDB

number 24. Or there can be many residues with the same PDB number but different insertion codes.

To renumber sequences

1. Choose **Edit | Resequence PDB numbers** to display the PDB number above each residue.

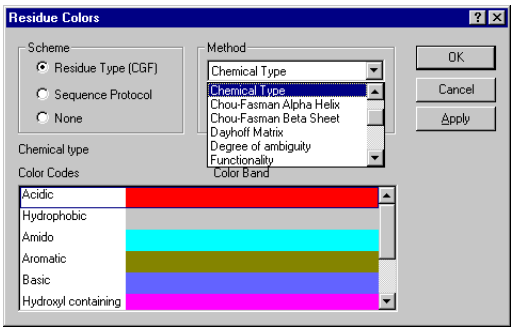
   Renumbering replaces all PDB numbers in the sequence with the current numbers in the sequence ruler.

Coloring sequences by properties

To color a sequence

1. Choose **View | Residue Colors...**

   The Residue Colors dialog appears.



2. Choose the color Scheme:
   - Residue Type
   - Sequence Protocol
3. Choose the Method.

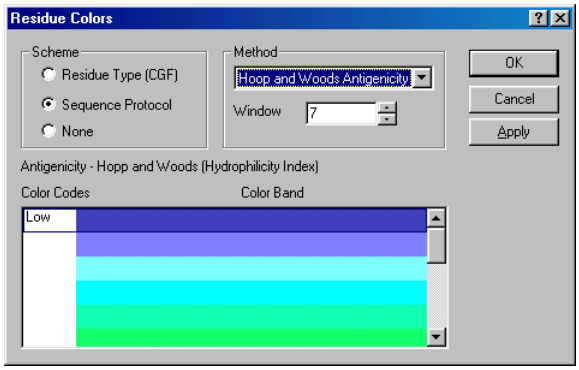
Method details are explained in Chapter , *"Understanding Sequence Property Predictions"*

The method window specifies the number of adjacent residues that are grouped together for analysis. For example, a window of 17 will result in the sequence being analyzed in blocks of 17

residues to determine properties such as the antigenicity or hydropathy.

A coloring legend showing the resulting color scheme displays in the bottom half of the dialog box.

For example, if you color by sequence protocol, you see this dialog.



4. Click **Apply** to color all residues in the sequence view without closing the dialog. Click **OK** to color all residues and close the dialog.

   For some residues and some types of properties, the property value cannot be determined because the sequence may be too short. Residues for which the property cannot be determined are colored white.

To display the property legend

1. In the Sequence View window, choose **View | Property Legend**.

   The Property Legend is available when residues are colored by sequence protocol and the residues have different colors.

Wrapping and hiding sequences

To wrap sequences

1. Check **Format | Wrap Lines** to display all sequences folded at the window boundary.

To unwrap sequences

1. Uncheck **Format | Wrap Lines** to display all sequences on a single line that can be scrolled.

.

To hide a sequence

1. In the Sequence View window, select the name of the sequence you want to hide.
2. Choose **View | Hide Sequence** to hide the sequence.

   Alternatively, close all 3D structure and sample property windows for the biomolecule. The sequence for the structure is removed from the sequence view.

.

To display the sequence again

1. Choose **Analyze | Sequence** in the 3D structure window.

Changing biomolecules

You use the CAChe sequence window to edit, modify, delete, mutate, build and analyze biomolecules at the secondary structure level.

As you modify your molecules, keep the following tips in mind:

- Commands from the **Edit** menu work on the active sequence only. The name of the active sequence is highlighted in yellow.
- Editing operations immediately change the 3D structure.
- You should tile your windows so that you can see the structure in a 3D workspace while making editing changes.
- Deleting residues deletes the residue group, its atoms, its bonds and other dependent objects. Inserting residues adds the residue group and all atoms and bonds belonging to that residue.
- Inserting residues in the middle of a sequence will shift the right most portion of the chain, changing the 3D coordinates of all atoms in the right subchain.
- Changing the Phi or Psi value of a residue may change the global 3D structure.

Mutating residues

Replacing residues causes a point mutation.

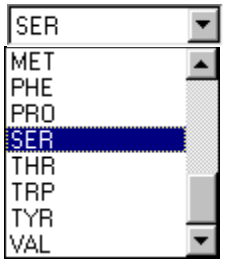
To mutate residues



1. Use the select tool to select the residues you want to mutate to a particular residue.

   The residues are highlighted. If the workspace is open on this structure, the atoms belonging to the selected residues are highlighted in the workspace.

2. Choose the new residue from the Residue Type drop-down.



The selected residues are replaced with the newly chosen residue.

NOTE When you mutate a residue, the backbone atoms of both residues are superimposed and then the original residue is removed. The residue in the workspace and the residue in the repository must contain the three crucial backbone atoms given by the PDB names (C, CA, N). If the backbone atoms are not present, a dialog appears that explains which residue was missing the backbone PDB names.

Inserting residues

To insert a residue



1. Select the name of a protein to activate it for modification. The name is highlighted in yellow.
2. In the Sequence View window, use the residue tool to select the position where the insertion is to take place.

   The insertion position is shown with an I-beam cursor between residues. If the workspace is open on this structure, the workspace display remains unchanged.
3. Do one of the following:
   - Type the 1-letter code for new residue
   - Choose **Edit | Insert** to insert the residue shown in the Residue Type box in the style bar.

   The new residue is inserted at the insertion position and the I-beam moves to the right.

📖 NOTE When you insert a residue the Psi and Phi angles used are the same as specified in the style bar. In addition, the next residue in the sequence is moved to make room for the insertion only if the peptide bond is shorter than 2 A.

Deleting residues

To delete residues

Do one of the following



1. Use the Select tool to select the residues you want to delete.

   The selected residues are highlighted. If the workspace is open on this structure, the atoms belonging to the selected residues are highlighted in the workspace.

2. Type the Delete key.

   The selected residues are deleted and a single asterisk appears in place of the deleted residues. The chain is broken unless the deleted residues were at the end of a chain.

Or



1. Use the Residue tool to place the I-beam to the right of the residue you want to delete.
2. Type the backspace key.

   The residue to the left of the I-beam is deleted, the I-beam is moved to the left and a single asterisk appears in the place of the deleted residue. The chain is broken unless the deleted residues were at the end of a chain.

Joining chains

Chains are broken when you delete residues.

To join two chains



1. With the Select tool choose the two residues you want to join. One residue must be at the start of a chain and the other at the

end of a chain. The residues can be in the same chain.

The selected residues are highlighted. If the workspace is open on this structure, the atoms belonging to the selected residues are highlighted in the workspace.

2. Choose **Edit | Connect Chains**.

The selected residues are joined and the original chains are connected into one chain. No atoms are moved and, since the geometry is unchanged, unusually long bonds may be created. To clean up the structure after all modifications are made, run an experiment that optimizes the geometry.

To join adjacent chains



1. With the Residue tool place the I-beam to the right of the asterisk separating the chains you intend to join.
2. Type the Backspace key.

The asterisk disappears and two chains are joined forming one chain. No atoms are moved and, since the geometry is unchanged, unusually long bonds may be created. To clean up the structure after all modifications are made, run an experiment that optimizes the geometry.

Copying and pasting sequences

You can copy and paste selected residues within or between sequences. Pasted residues are inserted as new chains.

Building peptides and proteins

To build a peptide



1. In the Sequence View window, click the name of the chemical sample to activate it for modification. The sequence name is highlighted in yellow.
2. Choose the Residue tool.

   A flashing I-beam cursor appears at the beginning of the sequence.

3. Type the 1-letter code for each residue in the peptide or protein.

The new residue is inserted at the cursor creating a new chain. The box moves to the right and contains an asterisk that indicates the end of the chain.

The 3D structure displayed in the workspace is updated to contain the new residue. The new chain is added to the workspace away from any other structures.

📖 NOTE When you add a residue, the Psi and Phi angles used are the same as specified in the ribbon.

Building by homology

Since genes have changed through evolution, proteins are usually members of families of related proteins that have similar sequences and 3D structures. As a result, it is possible to predict an unknown structure from its sequence by using the X-ray structure of a homologous protein.

If you have the sequence for a protein with an unknown 3D structure and you have a homologous protein with a 3D structure, you can build the unknown 3D structure from the known one. You do this by editing the sequence of the homologous 3D structure so that it matches the sequence of the unknown.

To build by homology

1. Open the known protein in the workspace.
2. Choose **Analyze | Sequence** to display the sequence in the Sequence View window.
3. In the Sequence View window, replace, delete or add residues with ones from the new sequence.

   When you replace a residue, backbone atoms of both residues are superimposed and then the original residue is removed conserving the secondary structure.

📖 NOTE When the unknown sequence has extra residues that are not in the known structure, you will want to add them as loops.

To add loops without moving the other atoms in a chain, you break the chain at the point of loop insertion, then insert the residues forming the loop and finally rejoin the chain.

To insert a loop



1. In the Sequence View window, click the name of the chemical sample to activate it for modification. The sequence name is highlighted in yellow.
2. Use the Select tool to select the two residues where you want to insert the loop.
3. Select **Edit | Break Chain**. The chain is broken and an asterisk appears between the selected residues.



4. Use the Residue tool to add new residues to each chain in a loop.

   As you add residues, adjust the Psi and Phi angles so that new loop residues are added in the appropriate empty space and do not overlap existing residues. To view the sequence and 3D structure simultaneously, select **Window | Tile** to display the Sequence View window and the workspace side by side.
5. After all residues are added, place the Residue tool to the right of the asterisk and press the backspace key. The chains are rejoined and the asterisk disappears.

forming the loop and finally rejoin the chain.

To create a turn



1. In the Sequence View window, click the name of the chemical sample to activate it for modification. The sequence name is highlighted in yellow.
2. Use the Select tool to select the two residues where you want to place the turn.
3. Select **Edit | Make turn** and choose one of the following
   - Type I
   - Type I'
   - Type II
   - Type II'

The selected turn is created using angles in the selected residues

	Left Residue		Right Residue	
Type	**Psi**	**Phi**	**Psi**	**Phi**
I	-60	-30	-90	0
I’	60	30	90	0
II	-60	120	80	0
II’	60	-120	-80	0

Changing secondary structure

You can change the secondary structure or protein conformation from the style bar in the Sequence View window.

To change secondary structure



1. Use the Select tool to select the residues you want to adjust.

   Selected residues are highlighted. If the workspace is open on this structure, the atoms belonging to the selected residues are highlighted in the workspace. Secondary structure patterns are created by more than one adjacent residue.

2. Choose a secondary structure option from the secondary structure drop down in the style bar at the top of the Sequence View window.

The Phi and Psi angles are set to the values for the secondary structure and the residue geometry is changed to the new values.

To adjust Phi and Psi angles



1. Use the Select tool to select the residue you want to adjust.

   The selected residue is highlighted. If the workspace is open on this structure, the atoms belonging to the selected residue are highlighted in the workspace.

2. Type the new angles into the Phi or Psi boxes in the style bar at the top of the Sequence View window.

The residue geometry is changed.

📖 NOTE When you change the Psi and Phi angles of a residue, there can be large global effects on the protein.

Comparing biomolecules

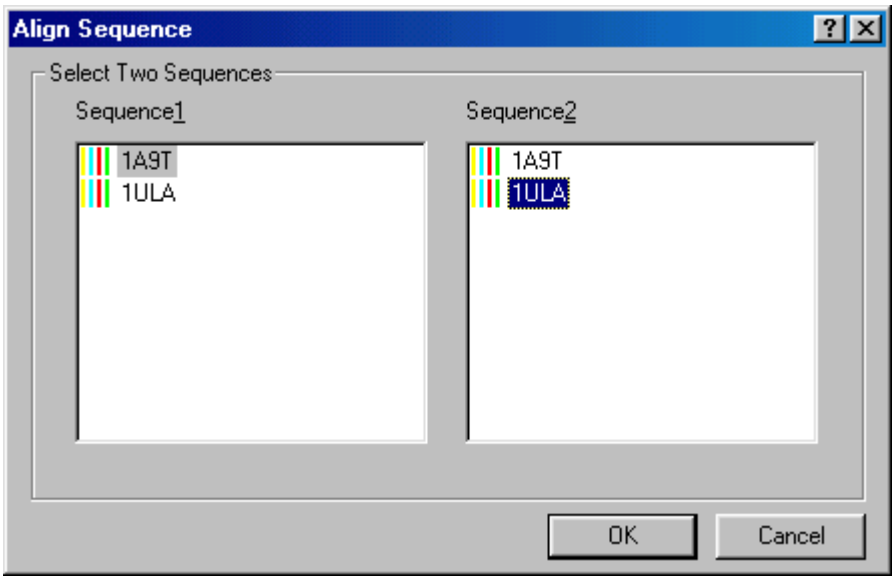
Aligning sequences

You can compare sequences to discover similarities in their structure and thus their function. To do so you can align sequences by placing gaps in the sequences.

To align a sequence automatically

1. Open the sequences of two or more chemical samples as described in *"Viewing sequence residues"*, p 9-18.
2. From the Sequence View window, choose **Edit | Align**.

   The Align Sequence dialog appears.



3. Choose a different sequence from each list and select **OK**.

   An exact pairwise sequence alignment is performed between the two selected sequences using the Needleman-Wunsch algorithm with BLOSUM50 matrix. Gaps are inserted between residues to bring the sequences into alignment.

You may adjust the alignment manually by inserting gaps as appropriate.

To align a residue manually

1. Open the sequences of two or more chemical samples as described in *"Viewing sequence residues"*, p 9-18.
2. With the Residue tool, place the flashing I-beam where you want to insert the gap.



3. Type either the space bar or the minus symbol (-) for each new gap you want to insert.

   New gaps are inserted to the left of the I-beam cursor. No changes are made to the 3D structure in the workspace.

To delete a gap

1. With the Residue tool, place the I-beam cursor to the right of gaps you want to delete.



2. Type the backspace key to delete the gap. No changes are made to the 3D structure in the workspace.

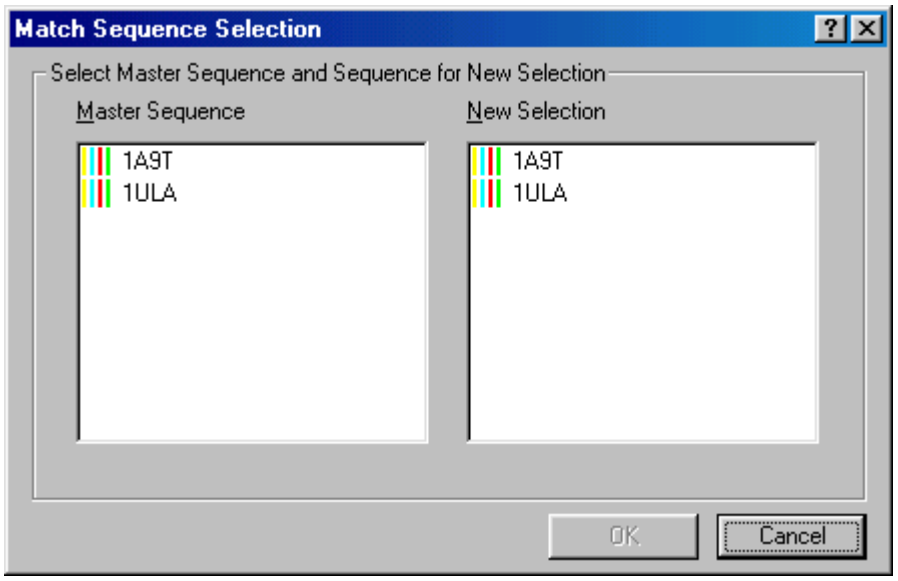
Matching selections

The active sites in homologous proteins are often conserved. When you have two aligned homologous proteins and the active site in one is selected, you can identify the active site in the second protein by selecting the matching residues.

To match a sequence selection

1. From the Sequence View, choose **Edit | Match Selection**.

The Match Sequence Selection dialog appears.



2. Chose one sequence from each list. The Master Sequence contains the selection you wish to match in the New Selection.

   The **OK** button highlights.

3. Select **OK**.

   The dialog closes and residues in the New Selection sequence adjacent to selected residues in the Master Sequence highlight and all other residues dim.

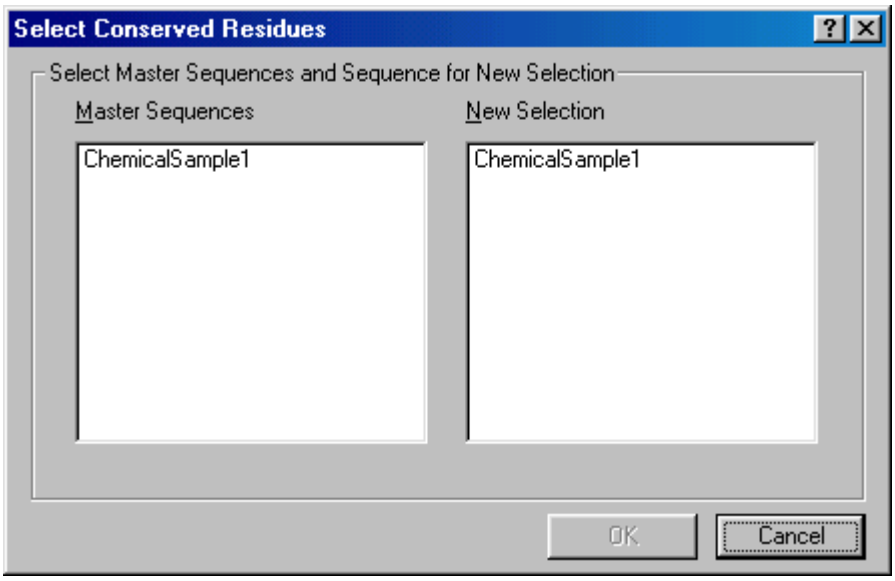
Select conserved

The active sites in homologous proteins are often conserved. When you have many aligned homologous proteins, you may be able to identify the active site residues in them protein by selecting the conserved residues.

To select conserved residues

1. From the Sequence View, choose **Edit | Select Conserved**.

The Select Conserved Residues dialog appears.



2. Chose one or more sequences from each list. Choose the sequences whose residues are to be matched from the Master Sequence and choose the sequences that will have the conserved residues highlighted from the New Selection list. You may choose the same sequences in each list.

   The **OK** button highlights.

3. Select **OK**.

   The dialog closes and residues in the New Selection sequence that are conserved in all the sequences from the Master list and the New Selection list highlight. All other residues dim.

Superimposing biomolecules

You can compare the molecular geometry of two biomolecules by superimposing one or more residues from one onto the corresponding residues in the other.

CAChe superimposes the C_α atoms of the selected residues from both biomolecules to coincide with each other as much as possible.

You can then compare any differences in structural geometry, indicated by the RMS label displayed in the workspace.

To superimpose two molecules by residue

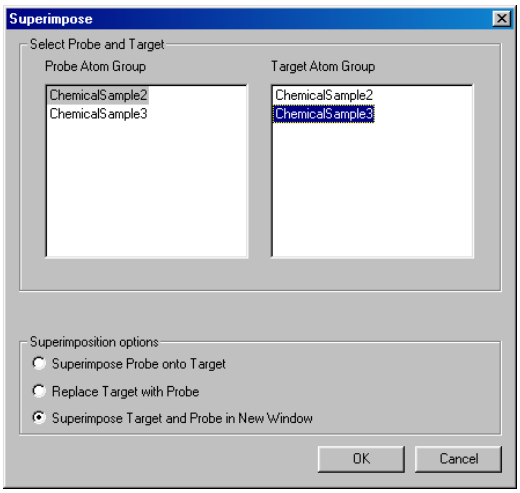


1. Select the residues that you want to be superimposed on another structure's residues by clicking on the residues in the sequence window with the Select tool.

NOTE Only sequences from two different chemical samples can be superimposed. The order in which residues are selected is not important.

2. Choose **Edit** | **Superimpose Sequences**.

   The Superimpose dialog box appears, which allows you to choose which chemical sample is the target, which is the probe, and where the superposition takes place.



   Choose the Superposition option to specify where the result appears. If you choose to Superimpose Target and Probe in a New Window, the new window is titled "Superposition Results".

   The probe chemical sample overlaps the target chemical sample in a workspace. The selected atoms are highlighted to show that they are selected. An RMS error is displayed in the workspace that indicates the error in molecular geometry between the C_α

Using

atoms in the selected residues.

Removing superposition

In the workspace, do one of the following to remove the superposition:

- Choose **Edit** | **Undo Superimpose**.
- Press **Ctrl Z**.
- Select one molecule by clicking on it with the Select Molecule tool and dragging to move the selected molecule to one side.

No undo is available if the superposition is done in a new window. Simply close the window without saving it to remove the superposition.

Extending the amino acid repository

By default the amino acid (AA) repository consists of the templates for the 20 standard amino acids. Each of the standard amino acids has the 1-letter code of the amino acid assigned as a keyboard shortcut. The shortcut allows you to build a sequence by typing 1-letter codes on the keyboard.

You may extend the repository by adding nonstandard amino acids and assigning shortcuts to them. After adding the nonstandard amino acid to the repository, you can used it for building peptide sequences in the same way as the standard amino acids.

You add nonstandard amino acids to the repository in one of two different ways:

- directly from the Sequence View of a PDB file
- from the Sequence View of a nonstandard amino acid you have drawn in the CAChe Workspace

Nonstandard amino acid in a PDB file

With CAChe, you can easily add nonstandard residues that appear in PDB files.

To add a nonstandard residue from a PDB file

1. From the 3D Structure window, choose **File | Open** and select the PDB file containing nonstandard amino acids.

   The PDB file opens in a new 3D Structure window.

TIP If you need a trial case, 4hvp.ent contains the following hetero groups:

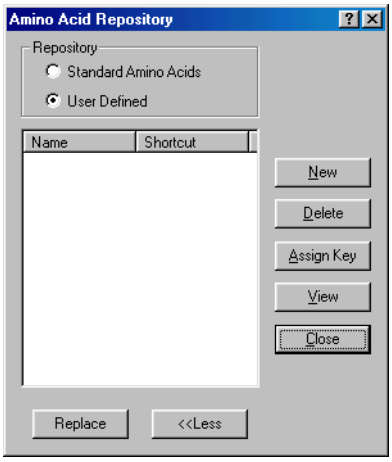
```
ABA - ALPHA-AMINO-N-BUTYRIC ACID
NLE - NORLEUCINE
```

2. Choose **Analyze | Sequence**.

   The Sequence View window comes to the front and the sequence from the PDB file appears.

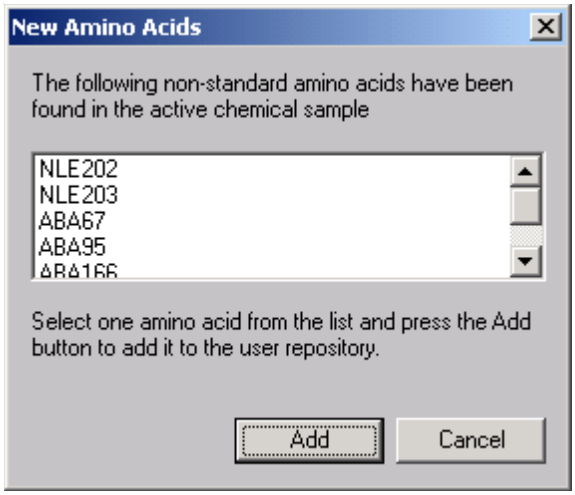
3. Choose **Options | Amino Acids Repository.**

   The Amino Acids Repository dialog appears.



4. In the Amino Acids Repository dialog, press the **New** button

   The New Amino Acids dialog appears:



5. Select one amino acid, e.g. ABA67, from the New Amino Acid list and choose **Add**.

   The selected residue is added to the repository, displayed in the Amino Acid list and available in the Residue Combo Box.

Creating and adding a nonstandard amino acid with the Workspace

1. In the CAChe 3D Structure window, build a nonstandard amino acid.

TIP

Amino acids in the repository are building blocks that appear in repeat units in the sequence. For example, the repository contains the glycyl fragment, not glycine. Amino acids also must contain the N-C-C- backbone.

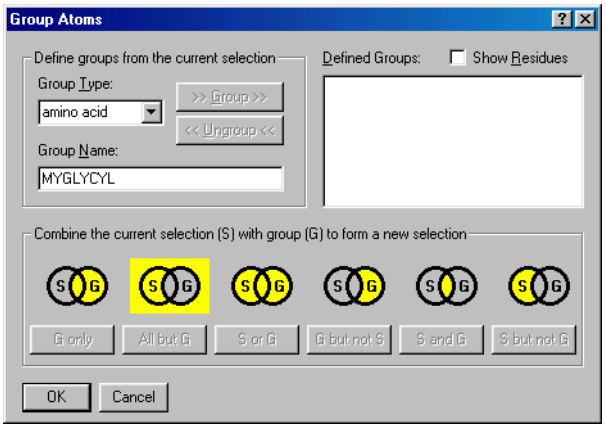
2. Choose **Beautify | Valence**.

   Hydrogen atoms are added.

3. Choose **Edit | Group Atoms**.

   The Group Atoms dialog box appears.

4. Choose amino acid from the **Group Type** pull down and type In the group name into the **Group Name** text box, and press the **>>Group>>** button.



   The group appears in the **Defined Groups** list.

5. Click **OK**.

   The Group Atoms dialog box closes.

6. Choose **Analyze | Chemical Properties Spreadsheet** and click the **Groups** tab.

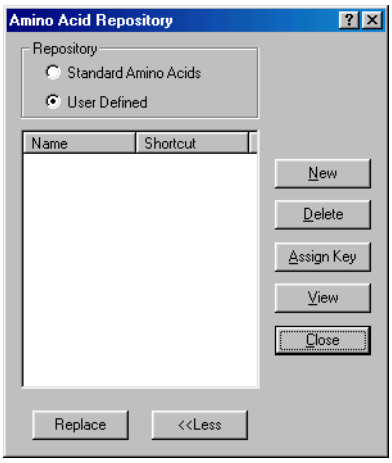
   The chemical properties workbook opens and the Groups page is at the front. Check that:

- The group type is AA_GROUP,
- the group name is as you typed it,
- and the group PDB Name is the first 3 letters of the group name.

7. Close the Sample Properties Window.
8. In the 3D Structure window, select **Analyze | Sequence**.

   The Sequence View comes to the front with the sequence of the chemical sample.
9. Choose **Options | Amino Acids Repository**.

   The Amino Acids Repository dialog appears.



10. In the Amino Acids Repository dialog, press the **New** button.

    The New Amino Acids dialog appears.
11. Select the available item that contains the name of the new amino acid group that you created and click **Add**.

    The selected residue is added to the repository and the dialog closes. The new amino acid is displayed in the Amino Acid list and available in the Residue Combo Box.

10 Performing Workspace Experiments

Overview

This chapter describes experiments in the CAChe workspace, including:

- an overview of the experimental properties and procedures available in CAChe, and the computational applications involved in each experiment
- a detailed description of how to perform a CAChe experiment in the workspace
- an overview of all experiment files that CAChe creates, their file names, and file locations.



Refer to Chapter 11, *"Using the Procedure Editor"*, for details about creating new experiments, Chapter 12, *"Using ProjectLeader"*for an overview of performing experiments using ProjectLeader, and *"Workspace versus ProjectLeader"*, p 2-21, for a comparison of the two.

Contents

Introduction to workspace experiments 10-2
Setting up a workspace experiment 10-4
Preparing a chemical sample file 10-4
Choosing a property class 10-5
Choosing a property 10-5
Choosing a procedure 10-9
Choosing a server 10-17
Running an experiment 10-18
Saving an experiment file 10-23
Stopping an experiment 10-24
Running experiments simultaneously 10-26
Viewing active experiments 10-27
Viewing server information 10-29
Size and element limitations 10-31
Troubleshooting experiments 10-32
Reattempting output file generation 10-32
Displaying servers on which to run an experiment 10-33
Displaying experimental details 10-35
Viewing experimental results 10-36
Sample.io folder 10-37
Sample.iso folder 10-37
Sample.map folder 10-39
Viewing log files and output files 10-40

Introduction to workspace experiments

CAChe runs experiments by performing calculations based on the geometry or molecular properties of a chemical sample in the workspace.

Workspace experiments allow you to visualize experimental results in a variety of ways such as:

- viewing low-energy conformations alongside a three-dimensional energy graph
- animating a series of low-energy structures
- superimposing surfaces on a molecule, representing electronic properties such as electron density or susceptibility to attack.

The calculations are performed by a range of computational applications, which apply mathematical models from classical mechanics, quantum mechanics, and dynamics to the chemical sample in the workspace.

Workspace experiments generate the following types of information:

- low-energy conformations of your molecule
- the geometry of a series of low-energy conformations, mapped against energy in a two- or three-dimensional graph
- distribution of electronic properties of your chemical sample, calculated as a shaded surface superimposed on the molecule
- atom and bond properties, including partial charge, bond order, and bond strain
- transition state and reaction path conformations of your molecule
- infrared (vibrational) and UV-visible (electronic) spectra, with motion vectors or molecular orbitals superimposed on a molecule in the workspace for any transition in the spectra.

Some CAChe experiments produce complicated three-dimensional output, or a large amount of textual information, which is saved in a new output file based on the name of the original chemical sample file.

CAChe performs experiments locally on your computer, unless you have access to a Unix-based CAChe GroupServer.



Refer to Chapter 11, *"Using the Procedure Editor"*, for details about creating new experiments, modifying procedures, and editing parameter data sets.

Refer to *"Setting up a workspace experiment"*, p 10-4, for a full list of the properties and procedures that you can use in experiments, and which procedures to use for a certain type of experiment.

Refer to *"Viewing experimental results"*, p 10-36, for details on file types generated by different experiments, and the content of a file type.

Refer to Chapter 20, *"CAChe Computational Applications"*, for detailed information on the computational applications that CAChe uses.

Setting up a workspace experiment

The following steps outline the process of performing a workspace experiment, and the properties and procedures available.

1. Prepare a chemical sample file.
2. Choose a property class to investigate.
3. Choose a property to investigate.
4. Choose a procedure to use.
5. If you have access to CAChe GroupServer, choose a server to run the experiment on.



Refer to Chapter 11, *"Using the Procedure Editor"*, for details about creating a new experiment.

After these steps just listed, you are ready to start the experiment.



Refer to *"Running an experiment"*, p 10-18, for details about performing an experiment in CAChe.

Preparing a chemical sample file

Before you can perform an experiment, you need to build and investigate the geometry of your molecule in a chemical sample file.

Perfect the geometry of the molecule as much as possible by using the tools and menu options in the workspace before running an experiment.

Some CAChe experiments, such as generating an energy map, also require the addition of search labels.



Refer to Chapter 4, *"Creating Chemical Samples"*, and Chapter 5, *"Modifying Chemical Samples"*, for details about building and perfecting your molecule.

Refer to Chapter 8, *"Investigating Molecular Geometry"*, for details about adding geometry search labels to your molecule.

Choosing a property class

Choose from the following five classes of properties on which to experiment and investigate further for your chemical sample:

- chemical sample properties
- atom properties
- bond properties
- sample conformation properties
- reaction and transition state properties.

Choosing a property

The workspace provides a range of properties on which you can experiment for each class of property. Properties for each property class are described in the following sections.

Chemical sample properties

Choose from the following properties for a chemical sample.

Optimized geometry

Optimizes the geometry of your chemical sample using procedures from either classical molecular mechanics, or semi-empirical quantum mechanics. Procedures that use classical methods are the fastest and usually give good results. You can optimize a molecule to discover:

- low energy structures
- transition state structures, which can also be determined by investigating reaction properties.

Heat of formation

Calculates the energy of a chemical sample at a geometry-optimized energy minimum.

IR transitions

Generates an infrared (IR) spectra for a molecule, created by coordinated motions of the atoms as electromagnetic radiation in the infrared region is absorbed by the molecule.

UV-visible transitions

Generates a UV-visible spectrum for a molecule, created by electron transition between molecular orbitals as electromagnetic radiation in the visible and ultraviolet (UV-visible) region is absorbed by the molecule.

📖 NOTE UV-visible spectra can be generated only if you have the optional VAMP add-on.

Current energy

Calculates the energy of the chemical sample at its existing geometry. The geometry of the sample is not changed by this experiment.

Electron density

Generates an electron density isosurface for an electron probability density of 0.01 e-/$Å^3$. The surface is colored to reflect the electrostatic potential at every point on the surface.

HOMO and LUMO

Calculates the energies and shapes of the HOMO and LUMO of your chemical sample using a quantum mechanical application.

HOMO-5 to LUMO+4

Generates the energies and shapes of a total of 11 molecular orbitals ranging from HOMO -5 to LUMO +4.

All molecular orbitals

Generates the shapes and energies of all of the molecular orbitals (MOs) in your chemical sample.

Electrostatic isopotential

Generates an electrostatic potential isosurface that shows both the polarity of the potential and where in space the potential equals ±0.03 a.u. (±18 kcal/mol, ±75 kJ/mol).

Susceptibility (electrophilic, nucleophilic, or radical)

Creates a three-dimensional surface superimposed over your chemical sample which indicates areas that are vulnerable to an attack by either electrophiles, nucleophiles, or radicals.

Superdelocalizability (electrophilic, nucleophilic, or radical)

Creates a three-dimensional electron density isosurface with colors reflecting the relative differences in reactivity of the different parts of your sample.

Atom properties

Choose the following property for an atom.

Atomic partial charge

Calculates atomic partial charges for every atom in your chemical sample.

Bond properties

Choose from the following properties for a bond.

Calculated bond order

Determines the computed bond order of every bond in your chemical sample using semi-empirical quantum mechanical methods.

Calculated bond strain

Determines the computed bond strain of every bond in your chemical sample using classical mechanical methods.

Chemical sample conformation properties

Choose from the following properties for a chemical sample conformation.

Rigid map

Generates a potential energy map of conformations determined by geometry search labels in the sample for each structural element you want to vary, with structures for each map point not optimized.

Optimized map

Generates a potential energy map of conformations determined by geometry search labels in the sample for each structural element you want to vary, with structures for each map point optimized.

Sequence of conformations

Generates a collection of low-energy conformations by sequentially searching an unlimited number of geometry labels. The resulting map file contains local energy minima, but does not offer information about the energy barriers between them.

Dynamics trajectory

Generates a trajectory of a chemical sample in random thermal motion by randomly adding kinetic energy to each atom. Motion is induced that can overcome small barriers to lower energy structures.

Reaction and transition state properties

Map reaction

Creates a transition state structure from a reactant and a product molecule of a chemical reaction.

Search for saddle

Locates a stationary point between the reactant and product that corresponds to the transition state for the reaction.

Refine transition state

Refines a transition state structure using a minimize gradient calculation.

Verify transition state

Verifies the current transition state geometry, where a single negative vibration confirms a true transition state.

Find reaction paths

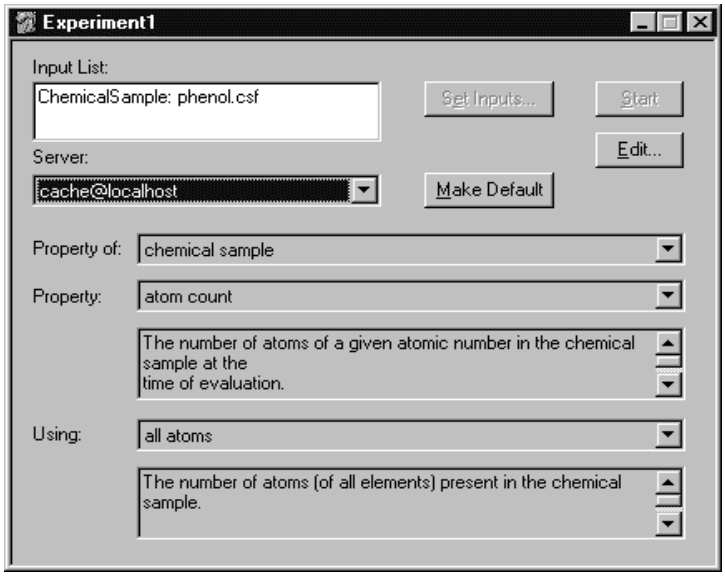
Produces an assemblage file containing the structures a chemical sample in a transition state geometry will pass through on the way to the reactant or product structures.

Choosing a procedure

The workspace offers a wide range of procedures that you can use to investigate a property. Procedures are applied by one or more of the computational applications, which apply theories from classical mechanics, quantum mechanics and dynamics to your chemical sample.

Identifying the procedure number

Each procedures you can use to run CAChe experiments applications involved in each procedure. Each procedure is identified with a number. This procedure number can be viewed in CAChe from the Experiment dialog box, displayed by choosing **Experiment | New**.



Example of an Experiment dialog box

The currently selected procedure is displayed in the **Using** box and a description of the procedure is displayed in the box underneath.

Select the down arrow to scroll to the bottom of the description, where a number is displayed. The last two digits of the four-digit number display the procedure number for the selected procedure.

For example, the procedure number of the example shown in the example dialog box earlier is 12.

Refer to *"Running an experiment"*, p 10-18, for details about how to use the Experiment dialog box.

Using the table of procedures

The following table lists the different procedures and the computational applications involved in each procedure.

The fastest quantum mechanical procedure for chemical sample, atom, and bond properties is usually procedure 3.

The most accurate quantum mechanical procedure for chemical sample, atom, and bond properties is usually procedure 8, although depending on your sample, 7 or 9 may yield better results.

To model your sample in water, choose procedures 4, 5, 10, 11, 14, 15, 18, or 19.

To model transition state geometries, choose procedures 16, 17, 18, or 19.

To generate additional surfaces for a chemical sample, when an experiment that uses one of the procedures numbered 1-19 has already been run on it, choose procedure 20. Procedure 20 takes advantage of geometry and wavefunction data generated already during the first experiment.

Procedure Number	**Procedure Name**	**Computational Applications**
0	MM geometry	Mechanics
1	MM geometry with AM1 wavefunction	Mechanics, MOPAC, Tabulator
2	MM geometry with PM3 wavefunction	Mechanics, MOPAC, Tabulator
3	MM geometry with EHT wavefunction	Mechanics, ExtHückel, Tabulator
4	MM geometry with AM1 wavefunction in water	Mechanics, MOPAC, Tabulator
5	MM geometry with PM3 wavefunction in water	Mechanics, MOPAC, Tabulator
6	MM geometry with INDO/1 wavefunction	Mechanics, ZINDO, Tabulator

Procedure Number	Procedure Name	Computational Applications
7	MM/AM1 geometry with AM1 wavefunction	Mechanics, MOPAC, Tabulator
8	MM/PM3 geometry with PM3 wavefunction	Mechanics, MOPAC, Tabulator
9	MM/INDO/1 geometry with INDO/1 wavefunction	Mechanics, ZINDO, Tabulator
10	MM/AM1 geometry with AM1 wavefunction in water	Mechanics, MOPAC, Tabulator
11	MM/PM3 geometry with PM3 wavefunction in water	Mechanics, MOPAC, Tabulator
12	AM1 geometry with AM1 wavefunction	MOPAC, Tabulator
13	PM3 geometry with PM3 wavefunction	MOPAC, Tabulator
14	AM1 geometry with AM1 wavefunction in water	MOPAC, Tabulator
15	PM3 geometry with PM3 wavefunction in water	MOPAC, Tabulator
16	AM1 transition state geometry with AM1 wavefunction	MOPAC, Tabulator
17	PM3 transition state geometry with PM3 wavefunction	MOPAC, Tabulator

Procedure Number	Procedure Name	Computational Applications
18	AM1 transition state geometry with AM1 wavefunction in water	MOPAC, Tabulator
19	PM3 transition state geometry with PM3 wavefunction in water	MOPAC, Tabulator
20	existing geometry and wavefunction	Tabulator
25	rigid or optimized map, unlimited search labels	Mechanics
26	AM1 rigid or optimized map, 1 search label	MOPAC
27	PM3 rigid or optimized map, 1 search label	MOPAC
28	AM1 rigid or optimized map, 2 search labels	MOPAC
29	PM3 rigid or optimized map, 2 search labels	MOPAC
30	AM1 rigid or optimized map, 1 search label, in water	MOPAC
31	PM3 rigid or optimized map, 1 search label, in water	MOPAC
32	AM1 rigid or optimized map, 2 search labels, in water	MOPAC
33	PM3 rigid or optimized map, 2 search labels, in water	MOPAC
36	single pass sequence of conformations, unlimited search labels	Mechanics

Procedure Number	Procedure Name	Computational Applications
37	multiple pass sequence of conformations, unlimited search labels	Mechanics
38	random motion at 300K, uses MM2 parameters	Dynamics
39	AM1 transition state, requires reactant and product as input	MOPAC
40	PM3 transition state, requires reactant and product as input	MOPAC
41	AM1 transition state in water, requires reactant and product as input	MOPAC
42	PM3 transition state in water, requires reactant and product as input	MOPAC
45	AM1 intrinsic reaction coordinate	MOPAC
46	AM1 intrinsic reaction coordinate, reverse direction	MOPAC
47	PM3 intrinsic reaction coordinate	MOPAC
48	PM3 intrinsic reaction coordinate, reverse direction	MOPAC
49	AM1 dynamic reaction coordinate	MOPAC
50	AM1 dynamic reaction coordinate, reverse direction	MOPAC
51	PM3 dynamic reaction coordinate	MOPAC

Procedure Number	Procedure Name	Computational Applications
52	PM3 dynamic reaction coordinate, reverse direction	MOPAC
55	MM/PM3 geometry with INDO/1 wavefunction	Mechanics, MOPAC, ZINDO, Tabulator
57	AM1 geometry with AM1 wavefunction	MOPAC, Tabulator
58	PM3 geometry with PM3 wavefunction	MOPAC, Tabulator
59	Current geometry with INDO/1 wavefunction	ZINDO, Tabulator

📖 NOTE Dynamics, MOPAC, and ZINDO are not available with Personal CAChe. MOPAC, ZINDO, and Extend Huckel are not available with BioCAChe.

Matching properties to procedures

The following table lists the five classes of properties, described earlier in *"Choosing a property"*, and the procedures you can use to run an experiment to calculate each property.

Properties	Available procedures
Chemical Sample Properties	
Optimized Geometry	0, 7-19
Heat of Formation	12-15
UV-visible transitions	55, 59
IR transitions	57, 58
Current Energy	0, 12-15

Properties	**Available procedures**
Electron Density	1-20
HOMO and LUMO	1-20
HOMO-5 to LUMO+4	1-20
All Molecular Orbitals	1-20
Electrostatic Isopotential	1-20
Susceptibility (Electrophilic)	1-20
Susceptibility (Nucleophilic)	1-20
Susceptibility (Radical)	1-20
Superdelocalizability (Electrophilic)	1-20
Superdelocalizability (Nucleophilic)	1-20
Superdelocalizability (Radical)	1-20
Atom Properties	
Partial Charge	1-19
Bond Properties	
Bond Order	1-19
Bond Strain	0
Chemical Sample Conformation Properties	
Rigid Map	25-33
Optimized Map	25-33
Sequence of Conformations	36-37
Dynamics Trajectory (not Personal CAChe)	38

Properties	Available procedures
Reaction and Transition State Properties	
Map Reaction (not Personal or Bio-CAChe)	26-33
Search for Saddle (not Personal or Bio-CAChe)	39-42
Refine Transition State (not Personal or Bio-CAChe)	16-19
Verify Transition State (not Personal or Bio-CAChe)	57, 58
Find Reaction Paths (not Personal or Bio-CAChe)	45-52

Choosing a server

If you are using your CAChe product as a standalone program, experiments are performed locally on your computer.

However, if you are using CAChe in conjunction with CAChe GroupServer, you may have access to multiple Unix servers on which you can run experiments. If this is the case, you need to choose a server before you run an experiment.

Running an experiment

This section describes how to run a CAChe experiment from the workspace, and how to use the menu options and dialog boxes involved in performing an experiment.

You do not need to open the chemical sample file that you want to experiment on before running an experiment.

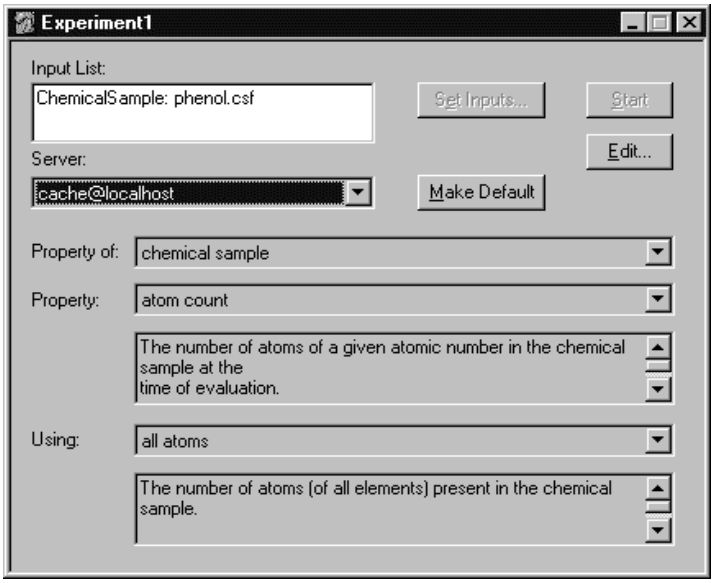
To perform an experiment

1. Do one of the following:



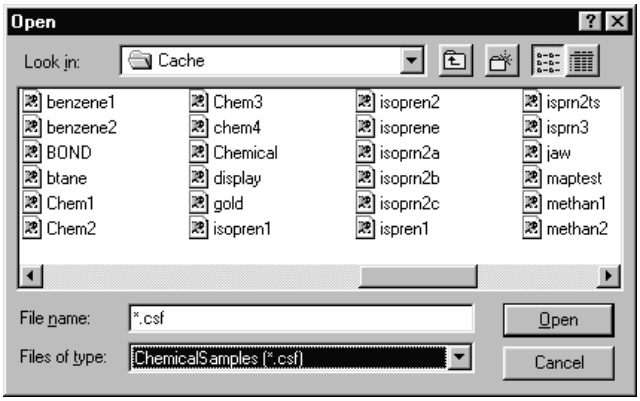
   - Choose **Experiment** | **New**.
   - Select the toolbar button shown to the left.

   The Experiment dialog box is displayed.



   The **Input List** box displays the name of the currently active chemical sample file.

2. If the file displayed in the **Input List** box is not the chemical sample file on which you want to perform the experiment, select the currently displayed file in the **Input List** file name, and select **Set Inputs** to display the Open dialog box.



3. Select the arrow button in the **Look in** box and choose **Cache** from the drop-down list to open the `Cache` folder.
4. Select the arrow button in the **Files of type** box and choose **Chemical Sample (*.csf)** from the drop-down list to display all chemical sample files in the `Cache` folder.
5. Do one of the following:
   - Click and drag on the scroll bar at the bottom of the scrolling list to locate the chemical sample file on which you want to experiment and select it by clicking on it.
   - Click in the **File name** text box and type the name of the chemical sample file on which you want to experiment.
6. Select **Open** to close the Open dialog box.

   The selected chemical sample file is now displayed in the **Input List** box in the Experiment dialog box.
7. Select the arrow button in the **Property of** box and choose the class of property on which you want to experiment from the drop-down list.

   For example, if you want to investigate the property of a chemical sample, choose **chemical sample** from the drop-down list.
8. Select the arrow button in the **Property** box and choose the property on which you want to experiment from the drop-down list.

For example, if you want to investigate the electron density of a chemical sample, choose **electron density** from the drop-down list.

The display box underneath the **Property** box describes the selected property.

9. Select the arrow button in the **Using** box and choose a procedure from the drop-down list.

   For example, if you want to use a procedure that applies MM geometry with a PM3 wavefunction, choose **MM geometry with PM3 wavefunction** from the drop-down list.

   The display box underneath the **Using** box describes the selected procedure, and the computational application that will perform the experiment.

   Refer to *"Choosing a property class"*, p 10-5, for a more detailed description of the selected property, and *"Choosing a procedure"*, p 10-9, for a more detailed description of the selected procedure.

10. Select the arrow button in the **Server** box and do one of the following:

    Choose **cache@localhost** from the drop-down list if you are using CAChe as a standalone CAChe product.

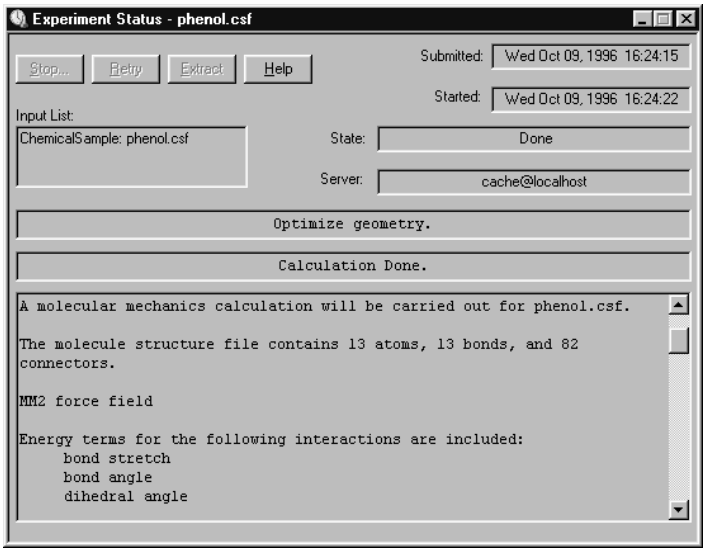
    Choose the remote server on which to run the experiment from the drop-down list if you are using CAChe in conjunction with CAChe GroupServer, and want to run the experiment on a remote CAChe server.

11. Select **Start** to begin the experiment.

    The Experiment Status dialog box is displayed, informing you of the following:

    - the name of the chemical sample file
    - the time and date when the experiment was submitted
    - when the experiment began executing
    - the server on which the experiment is running
    - the property being calculated
    - the experiment's progress as the calculations are performed

- the current computational application executing and the step it is performing.



The scrolling text window at the bottom of the Experiment Status window displays textual output received from the computational applications, and information on the progress of the experiment. Some common experimental states that you see during the course of an experiment are:

- **Pending**: The experiment has been submitted to your PC or to a remote server (if you are using CAChe with GroupServer), and the experiment is waiting to start because the server is busy with another experiment.
- **Executing**: The experimental property is currently being computed.
- **Returning Output Files**: The experimental results are being transferred into automatically generated files on your PC, or are being transferred from a remote server to your PC (if you are using CAChe with GroupServer).

The Experiment Status dialog box also displays information generated by the computational applications, such as steric energies, and heats of formation.

The relevant computational applications involved in the

experiment also appear minimized at the bottom of the CAChe application window in the Windows taskbar.

When the experiment is finished, the scrolling window in the Experiment Status dialog box displays the final results of the experiment and the time taken to complete the experiment. **Stop**, **Extract**, and **Retry** are disabled.

The relevant computational applications involved in the experiment no longer appear minimized at the bottom of the CAChe application window in the Windows taskbar.

12. Click and drag on the scroll bar of the scrolling window to view all the details of the experiment.

    Save this information by clicking and dragging with the cursor to select all the text in the window and choosing **Edit | Copy**. You can now paste the text into any text editor or word processor document.

    CAChe has also automatically saved this information in one or more log and output files located in an automatically generated input/output (`.io`) folder.

    Refer to *"Viewing log files and output files"*, p 10-40, for information on viewing log files.

13. When you have finished viewing the experimental details, select the Windows Close button in the upper right corner of the Experiment Status dialog box to close the dialog box.

    You return to the Experiment dialog box.

14. Do one of the following:

    - Save the settings in the Experiment dialog box, as described in the next section, *"Saving an experiment file"*.
    - Select the Windows Close button in the upper right corner of the Experiment dialog box to close the dialog box without saving its contents.

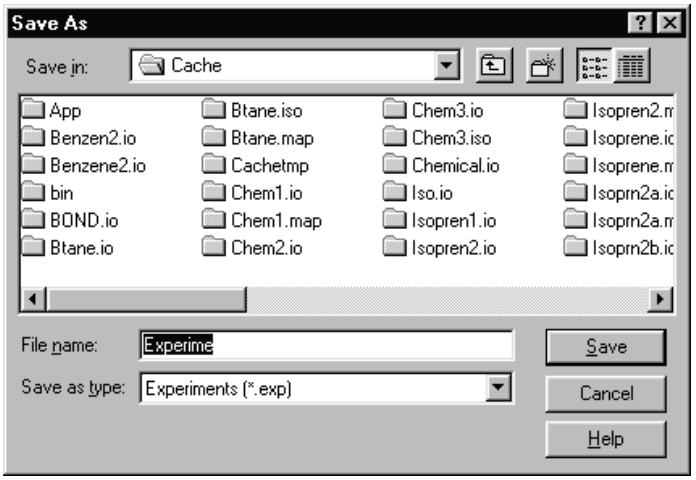
Saving an experiment file

You can save the settings in an Experiment dialog box as an experiment file (`*.exp`), so that you can reuse the same property and procedure settings without having to reselect any of the drop-down list options.

The next time you want to run an experiment with the same settings, open the `.exp` file to display the Experiment dialog box with the settings you saved.

To save an experiment file

1. Select the Experiment dialog box by clicking on it.
2. Choose **File** | **Save** to display the Save As dialog box.



3. Select a folder in which to save the experiment file from the **Save in** drop-down list or from the scrolling list.
4. Click in the **File name** text box and type a name for the experiment file you are saving.
5. Select the arrow button in the **Save as type** box and choose **Experiments (*.exp)** from the drop-down list.
6. Select **Save** to save the experiment file and to close the Save As dialog box.

   The file is saved with the extension `*.exp`.

Using

Stopping an experiment

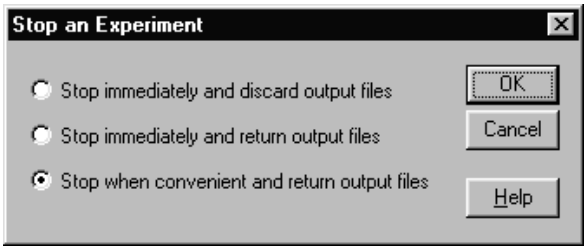
You can stop an experiment while it is still running before calculations are complete, and choose how to deal with any data already produced by the experiment.

You can stop an experiment from the following dialog boxes:

- the Experiment Status dialog box, displayed automatically while an experiment is running
- the Experiments Submitted dialog box, displayed by choosing one of the following:
  - **Experiment | Show Submitted Experiments**
  - **Experiment | Show Server Information**.

To stop an experiment from the Experiment Status dialog box

1. Select **Stop** to display the Stop an Experiment dialog box.



2. Select one of the following:

   Select the **Stop immediately and discard output files** radio button to stop the experiment immediately without returning any computational results. Your chemical sample input file is not altered. Any files that would have been overwritten by the calculation, such as map documents, tabulated orbital information, or computational output files, are untouched.

   Select the **Stop immediately and return output files** radio button to return whatever results the experiment has generated up to that point. This option is not recommended because it does not allow the experiment time to “clean up” before returning results. Consequently, the data returned may not be valid.

Select the **Stop when convenient and return output files** radio button to stop the experiment at a logical point in the calculations and save the output files. This returns files just as if the experiment had completed.

3. Select **OK** to close the Stop an Experiment dialog box.

   The experiment is aborted and output data already generated is either discarded or saved, depending on the option you selected.

   If you chose to save output files, data already generated is also displayed in the Experiment Status dialog box.

To stop an experiment from the Experiments Submitted dialog box

1. Choose one of the following:

   - **Experiment | Show Submitted Experiments**

     The Experiments Submitted dialog box is displayed, which shows experiments submitted by a user.

   - **Experiment | Show Server Information**

     The Select a Server dialog box is displayed, which shows a list of servers.

     Select the server on which the experiment you want to stop is running, and select **OK**.

     The Experiments Submitted dialog box is displayed, which shows experiments running on that server.

2. Select the experiment you want to stop in the Experiments Submitted dialog box.
3. Select **Stop** to display the Stop an Experiment dialog box.
4. Select the required radio button, as described in the previous procedure, *"To stop an experiment from the Experiment Status dialog box"*.
5. Select **OK** to close the Stop an Experiment dialog box and to close the Experiments Submitted dialog box.

   The experiment is aborted and output data already generated is either discarded or saved, depending on the option you selected.

Running experiments simultaneously

You can perform more than one CAChe experiment at a time.

To start a new experiment while another experiment is running

1. Do one of the following to display another Experiment dialog box from which you can start the next experiment:
   - Select **Extract** in the Experiment Status dialog box of the current experiment.
   - Choose **Experiment** | **New**.
   - Select the toolbar button shown to the left.



   - Choose **File** | **Open** to open an Experiment dialog box or experiment file (`*.exp`) which you have previously saved.
2. Select a chemical sample file, property class, property and procedure from the Experiment dialog box and select **Start** as described in the previous section "Running an Experiment."

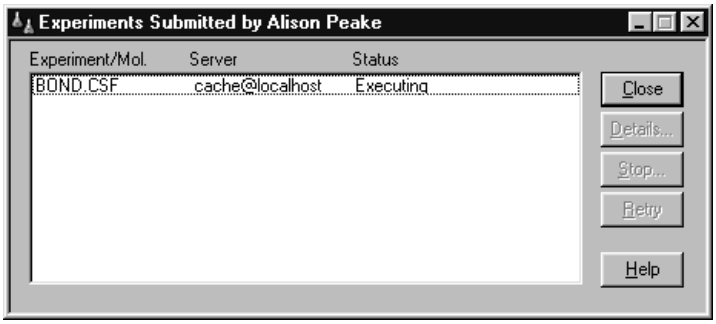
   The second experiment begins.

Viewing active experiments

You can view a list of experiments that have been submitted and are either currently being performed, or (if you are using CAChe in conjunction with GroupServer) experiments that are waiting for a free server.

To view submitted experiments

1. Choose **Experiments | Show Submitted Experiments** to display the Experiments Submitted dialog box.



   The Experiments Submitted dialog box displays experiments submitted by a user.

2. To view more detailed information on an experiment, select the experiment in the list and choose **Details**.

   The Experiment Status dialog box is displayed, which shows details of the calculations as they are performed, and the status of the experiment.

3. To stop an experiment, select the experiment in the Experiments Submitted dialog box and select **Stop**.

   The Stop an Experiment dialog box is displayed.

4. Select the required radio button, as described in the previous section, *"Stopping an experiment"*.

5. Select **OK** to close the Stop an Experiment dialog box and to stop the experiment.

6. To reattempt to generate output files if the experiment halts because of lack of storage space on your computer, select **Retry**.

Output file generation continues and output files are saved as normal.

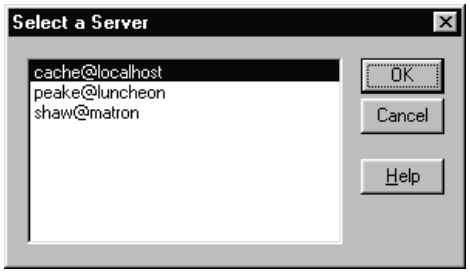
7. Select **Close** to close the Experiments Submitted dialog box.

Viewing server information

You can view a list of experiments being performed on a particular server. This is useful if you are using CAChe GroupServer with CAChe, so that you can see on which server active experiments are currently being processed.

To view server information

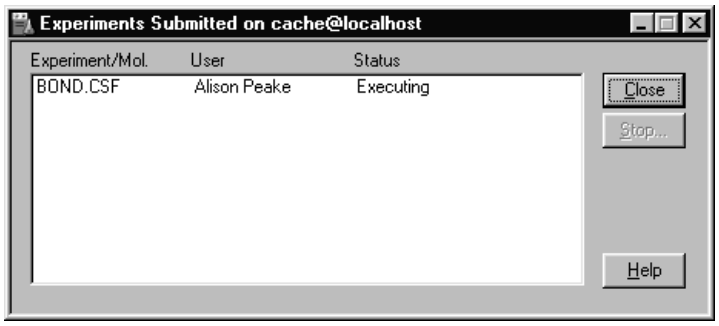
1. Choose **Experiment | Show Server Information** to display the Select a Server dialog box.



   The Select a Server dialog box lists available servers. If you are using CAChe as a standalone program, the list displays just **cache@localhost**.

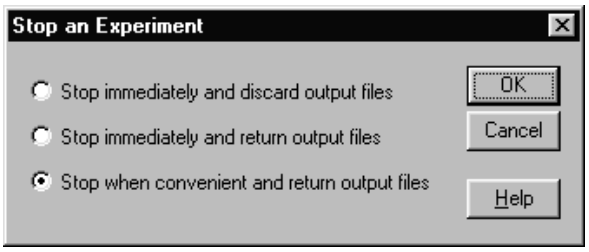
2. Select the server for which you want to view submitted experiments from the list, and select **OK**.

   The Experiments Submitted dialog box is displayed, listing experiments running on that server.



3. To stop an experiment, select the experiment in the list and choose **Stop**.

   The Stop an Experiment dialog box is displayed.



4. Select the required radio button, as described in the section *"Stopping an experiment"*, p 10-24.
5. Select **OK** to close the Stop an Experiment dialog box and stop the experiment.
6. Select **Close** to close the Experiments Submitted dialog box.

Size and element limitations

The size of your molecule might limit the experimental procedures that you can successfully execute.

Procedures that use MOPAC (for example, those that include AM1, PM3 or PM5 calculations) are limited by the amount of memory on your system. In practice, this means that MOPAC calculations are limited to molecules with 20,000 - 30,000 atoms or less.

Procedures that include INDO/1 calculations are limited to 200 atoms and 700 basis functions, where a basis function is equivalent to a valence atomic orbital. For example, carbon has four basis functions (one 2s and three 2p).

All other procedures are simply limited by the availability of memory.

The elements contained within your chemical sample file may limit your choice of procedures. Procedures that use the computational applications ExtHückel or Mechanics accept all elements.

📖 NOTE Procedures that use AM1, PM3, PM5 or INDO/1 parameters are not available with Personal CAChe or BioCAChe.

Troubleshooting experiments

This section outlines problems that you may encounter while trying to run CAChe experiments.

Reattempting output file generation

Occasionally, when an experiment is returning output files, your disk may fill up and the experiment will report an error because the output files cannot be saved.

CAChe enables you to make more disk space available and then continue to generate and save the output files.

You can reattempt to generate output files from the following dialog boxes:

- the Experiment Status dialog box, displayed automatically while an experiment is running
- the Experiments Submitted dialog box, displayed by choosing **Experiment | Show Submitted Experiments**

To reattempt output file generation from the Experiment Status dialog box

1. When you receive an error message that your disk is full, make more storage space available on your local computer.
2. Select **Retry**.

   Output file generation continues and output files are saved as normal.

To reattempt output file generation from the Experiments Submitted dialog box

1. When you receive an error message that your disk is full, make more storage space available on your local computer.
2. Choose **Experiment | Show Submitted Experiments**.

   The Experiments Submitted dialog box displays experiments submitted by a user.

3. Select the experiment you want to retry in the Experiments Submitted dialog box.
4. Select **Retry**.

   Output file generation continues and output files are saved as normal.

Displaying servers on which to run an experiment

When you choose **Experiment | New** to display the Experiment dialog box, you may find that the server you require is not listed in the **Server** drop-down list.

For example, if you are using CAChe as a standalone program, you need to select **cache@localhost** as the server on which to perform your experiment locally. If you are using CAChe with CAChe GroupServer, you need to select a GroupServer on which to perform your experiment.

If the server you require is not shown in the **Server** drop-down list of the Experiment dialog box, you need to edit your `tcpconf.txt` file, which is located in your `cache` folder.

For standalone users

If you are using CAChe as a standalone program and **cache@localhost** does not appear in the Experiment dialog box **Server** drop-down list, edit your `tcpconf.txt` file in the following way.

To edit the `tcpconf.txt` file to include a new server

1. Using a text editor, open your `tcpconf.txt` file, located in the CAChe directory.
2. Add the following to your `tcpconf.txt` file to include the `localhost` server on which to run CAChe experiments locally:
   - the keyword `server`
   - the server name of `localhost`
   - the login name of `cache`

- the keyword `CACH`
- the keyword `CalcManager`

The following shows an example `tcpconf.txt` file, with the server name `localhost` and login name `cache` added to the domain name server line.

```
# tcpconf.txt (TCP configuration file)
#
# Use these if the domain name server is available.
# keyword server_name login_name pc_ident unix_process_name
  server srvr1       jillj     CACH      CalcManager
  server localhost   cache     CACH      CalcManager
#
#
```

3. Save and close the `tcpconf.txt` file.
4. Quit and restart the CAChe application.

For users with access to GroupServer

For users who have access to CAChe GroupServer, and the servers on which you wish to run experiments do not appear in the Experiment dialog box **Server** drop-down list, you need to add the following to your `tcpconf.txt` file:

- the keyword `server`
- the name of the server or its IP address
- your login name on the server
- the keyword `CACH`
- the keyword `CalcManager`

The following shows an example `tcpconf.txt` file, with the servers `srvr1` and `srvr2` added to the domain name server line.

```
# tcpconf.txt (TCP configuration file)
#
# Use these if the domain name server is available.
# keyword server_name login_name pc_ident unix_process_name
   server localhost   cache     CACH      CalcManager
   server srvr1       jillj     CACH      CalcManager
   server srvr2       markp     CACH      CalcManager
#
#
```

5. Save and close the `tcpconf.txt` file.
6. Quit and restart the CAChe application.

Displaying experimental details

If you exit CAChe by mistake while an experiment is running, or if you accidentally close the Experiment Status dialog box while an experiment is in progress, you can redisplay experimental details.

To redisplay experimental details

1. Choose **Experiment | Show Submitted Experiments** to display a list of experiments in progress.
2. Select the experiment in progress whose details you want to view by clicking on it in the list.
3. Select **Details**.

   The Experiment Status dialog box is displayed, informing you of the experiment's progress.

Viewing experimental results

When you run an experiment in CAChe, a number of files containing experimental details are created and stored in automatically generated folders. The folders are prefixed with the same name as your chemical sample file. For example, if your chemical sample file is named `sample.csf`, the automatically generated folders are named as follows:

- `sample.io` (contains input/output files)
- `sample.iso` (contains isosurface files)
- `sample.map` (contains energy map files).

The following tables list all the files created by CAChe experiments, for a chemical sample file named `sample.csf`, and the location of the experimental files.

Sample.io folder

File name	Location	Creator	Type, Description
DYNAMICS.LOG	SAMPLE.IO	Dynamics	text, log file
DYNAMICS.OUT	SAMPLE.IO	Dynamics	text, output file
HUCKEL.LOG	SAMPLE.IO	ExtHückel	text, log file
HUCKEL.OUT	SAMPLE.IO	ExtHückel	text, output file
MECHANCS.OUT	SAMPLE.IO	Mechanics	text, output file
MECHANCS.LOG	SAMPLE.IO	Mechanics	text, log file
MOPAC.LOG	SAMPLE.IO	MOPAC	text, log file
MOPAC.OUT	SAMPLE.IO	MOPAC	text, output file
TABULATE.OUT	SAMPLE.IO	Tabulator	text, output file
ZINDO.LOG	SAMPLE.IO	ZINDO	text, log file
ZINDO.OUT	SAMPLE.IO	ZINDO	text, output file

Sample.iso folder

File name	Location	Creator	Type, Description
EP-DENS.ISO	SAMPLE.ISO	Tabulator	binary, electron density surface colored by electrostatic potential
NF-DENS.ISO	SAMPLE.ISO	Tabulator	binary, electron density surface colored by nucleophilic susceptibility (frontier density)

File name	Location	Creator	Type, Description
EF-DENS.ISO	SAMPLE.ISO	Tabulator	binary, electron density surface colored by electrophilic susceptibility (frontier density)
RF-DENS.ISO	SAMPLE.ISO	Tabulator	binary, electron density surface colored by radical susceptibility (frontier density)
NS-DENS.ISO	SAMPLE.ISO	Tabulator	binary, electron density surface colored by nucleophilic superdelocalizability
ES-DENS.ISO	SAMPLE.ISO	Tabulator	binary, electron density surface colored by electrophilic superdelocalizability
RS-DENS.ISO	SAMPLE.ISO	Tabulator	binary, electron density surface colored by radical superdelocalizability
ELEC.ISO	SAMPLE.ISO	Tabulator	binary, electrostatic potential isosurface
MO123.ISO	SAMPLE.ISO	Tabulator	binary, molecular orbital isosurface (orbital # 123)

Sample.map folder

File name	Location	Creator	Type, Description
ENERGY.MAP	SAMPLE.MAP	Mechanics MOPAC	binary, rigid or optimized map
DYNAMICS.MAP	SAMPLE.MAP	Dynamics	binary, Dynamics trajectory
SEQSRCH.MAP	SAMPLE.MAP	Mechanics	binary, sequence of conformations
IRC1.MAP	SAMPLE.MAP	MOPAC	binary, reaction path
IRC-1.MAP	SAMPLE.MAP	MOPAC	binary, reaction path
DRC1.MAP	SAMPLE.MAP	MOPAC	binary, reaction path
DRC-1.MAP	SAMPLE.MAP	MOPAC	binary, reaction path

Viewing log files and output files

Each CAChe computational application produces both a log file and output file when you use an experimental procedure that involves that computational application. The exception is Tabulator, which only produces an output file.

Log files (`*.log`) contain details such as the date and time of the experiment, computation time, and final result of the experiment. Output files (`*.out`) contain details of the calculations carried out on the chemical sample step by step, and the resulting values. You can view both log files and output files in any text editor or word processor.

Log files and output files are overwritten each time you perform another experiment on the chemical sample file using the same computational application. If you want to keep a particular experimental log or output file, save it under another name in your text editor or word processor.

11 Using the Procedure Editor

Overview

This chapter describes the Procedure Editor, and how to use it to:

- create a new experiment
- modify the settings of an experiment
- clone an existing experiment
- share experiments with other CAChe users.



Refer to Chapter 10, *"Performing Workspace Experiments"*, for an overview of performing experiments in the CAChe workspace.

Contents

The Procedure Editor 11-2
Starting the Procedure Editor 11-3
The Procedure Editor interface 11-4
The Navigator window 11-4
The Procedure window 11-6
The Parameter Data window 11-7
Managing the experiment environment 11-8
Using the tree view 11-8
Using the list view 11-11
Showing properties of a component 11-13
Available properties 11-14
Modifying a procedure 11-17
Adding a step 11-19
Deleting a step 11-19
Moving a step 11-19
Viewing the settings of a step 11-20
Calling a procedure 11-20
Running a procedure 11-21
Editing the settings of a compute engine 11-23
Creating experiments 11-25
Creating a new experiment 11-25
Cloning an existing experiment 11-27
Importing a CAChe experiment 11-28
Expert modification 11-30
Creating a group procedure package 11-31
Loading new packages 11-33
Refreshing the experiment environment 11-35
Returning to original settings 11-36
Exporting environment components 11-37
Quitting the Procedure Editor 11-38

The Procedure Editor

The Procedure Editor allows you to customize the procedure environment of the Workspace and ProjectLeader.

The Procedure Editor allows you to:

- edit procedures and other components of the experiment environment
- create new procedures and components of the experiment environment
- clone existing procedures
- share procedures with other CAChe users
- perform expert modification to individual property parameters
- create a new package of experiments, procedures, and parameter data for use by other users.

Starting the Procedure Editor

You can start the Procedure Editor in any of the following ways:

- manually from the **Start** menu
- from the Experiment Definition dialog box in the Workspace
- from the Property Wizard in the ProjectLeader.

To start the Procedure Editor

1. Perform one of the following:
   - From Windows, choose **Start | CAChe | Procedure Editor**
   - From the Workspace, select the **Edit** button in the Experiment Definition dialog box
   - From the ProjectLeader, select the **Edit** button in the Property Wizard.

   The Navigator window of the Procedure Editor is displayed.

   If you started the Procedure Editor from either the Workspace or the ProjectLeader, the Procedure Editor opens with the currently active experiment visible in the Navigator window, and the referenced procedure visible in a Procedure window.

   For experiments that are unique to the ProjectLeader, the Property dialog box is displayed instead.

The Procedure Editor interface

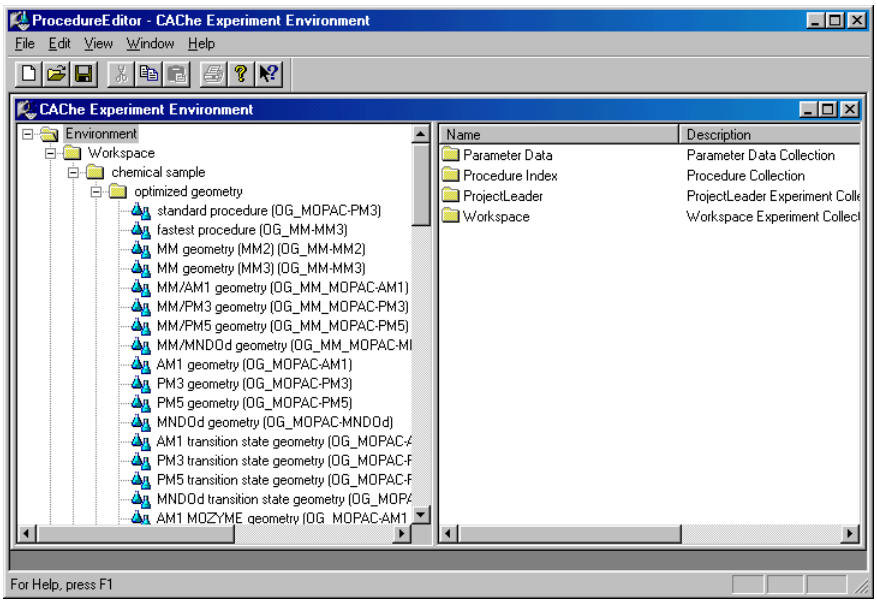
The Procedure Editor consists of three types of window:

- the Navigator window
- the Procedure window
- the Parameter Data window.

In addition, there is a menu bar and a toolbar. The menu bar changes as you select different types of Procedure Editor window.

The Navigator window

By default, the Navigator window is displayed when you start the Procedure Editor.



The Procedure and Parameter Data windows may be displayed by double-clicking an appropriate object in the Navigator window.

The Navigator window is divided into two panes:

- the left-hand side shows a tree view of the entire experiment environment
- the right-hand side lists the child components contained in the current folder.

Use the splitter bar between the two panes to adjust the portion of the screen filled by each pane.

The following symbols are used in the Navigator window to depict different types of object within the experiment environment:


a folder, usually containing other objects or sub-folders.


a CAChe experiment.

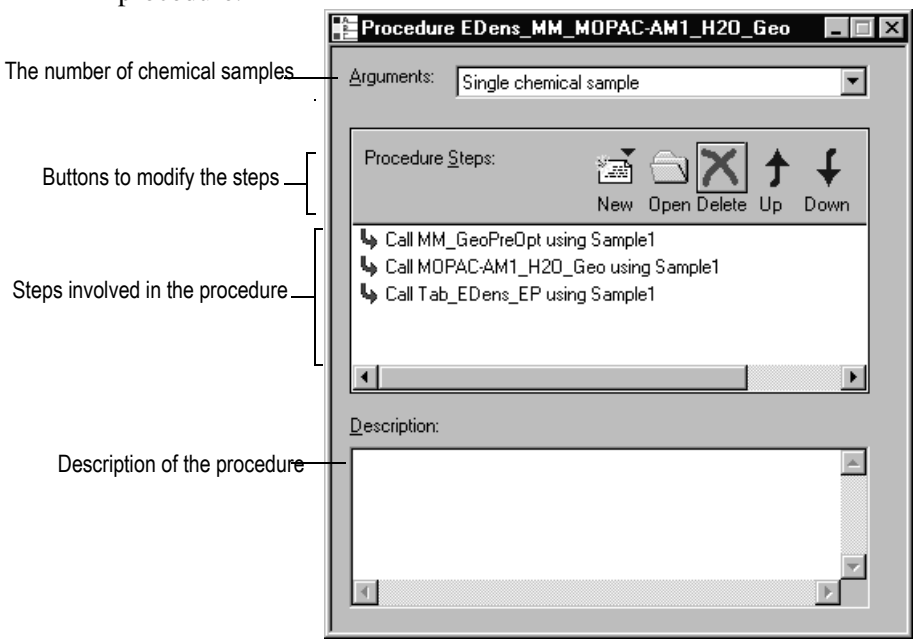

a procedure.


a parameter data set.

Refer to *"Managing the experiment environment"*, p 11-8, for details about managing experiments in the Navigator window

The Procedure window

The Procedure window dialog box allows you to modify the definition of a procedure. The title bar contains the title of the procedure.



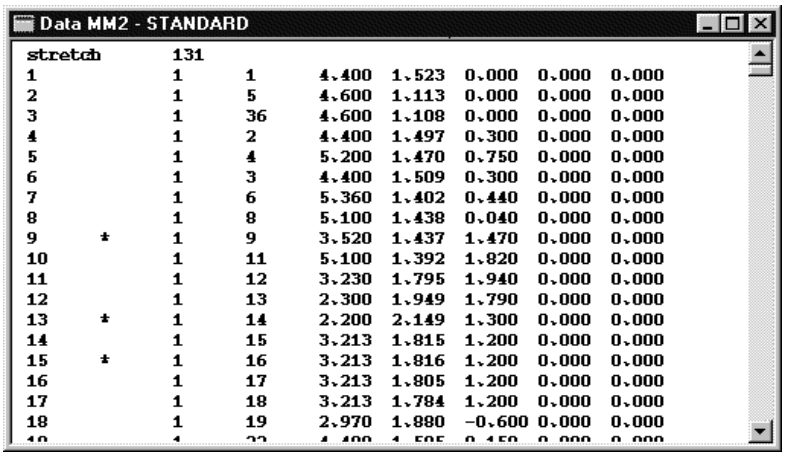
Use the five buttons in the Procedure Steps section to modify the existing procedure. In addition, you can use the menu options in the Procedure window to modify the procedure.

This dialog box is displayed from the Navigator window when you double-click on a procedure object in the tree view.

Refer to *"Modifying a procedure"*, p 11-17, for details about modifying procedures using this dialog box.

The Parameter Data window

The Parameter Data window lets you modify a parameter data set. The title bar contains the name of the data set displayed within the window.



Edit the figures in the window to change the parameter data set. If any unsaved changes have been made to the data set, the title bar displays an asterisk symbol (*).

This window is displayed from the Navigator window when you double-click on a data set object in the tree view.

Refer to *"Expert modification"*, p 11-30, for details about editing parameter data sets using this window.

Managing the experiment environment

This section outlines the ways in which you can manage the display of the experiment environment. This section details how to use the tree view and the list view of the Navigator window.

To display a new navigator window

- Choose **Window | New Navigator Window**.

A new navigator window is displayed in Procedure Editor.

Using the tree view

The following actions can be performed in the tree view:

- selecting an object in the tree view
- expanding and collapsing folders
- renaming objects
- displaying Procedure and Parameter Data windows.

Selecting an object

You can select a folder or an object within a folder.

To select an object in the tree view

- Position the cursor over the object and press the **left** mouse button.

NOTE When you have selected an object, press the **right** mouse button to display a pop-up menu containing a subset of the menu bar options for that object.

Expanding a folder

Expand a folder in the tree view to show all the subfolders nested beneath it.



The presence of subfolders is shown by a plus symbol (+) next to the main folder icon.

To expand a folder

1. In the tree view, move the cursor over the plus sign of the folder that you wish to expand.
2. Press the **left** mouse button to expand the selected folder.

NOTE Choosing **View | Expand All Folders** expands every object in the tree view.

Collapsing a folder

You can collapse a folder in the tree view to hide all the subfolders nested beneath it.



A folder that has been expanded is shown by a minus symbol (-) next to the main folder icon.

To collapse a folder

1. In the tree view, move the cursor over the minus sign of the folder that you wish to collapse.
2. Press the **left** mouse button to collapse the selected folder.

NOTE Choosing **View | Collapse All Folders** collapses all expanded objects in the tree view.

Renaming an object

You can rename an object in the tree view.

To rename an object

1. Select the object that you wish to rename.
2. Do one of the following:
   - Click on the selected object with the **left** mouse button.
   - Choose **File | Rename**.

   The object name is highlighted.
3. Enter a new name.

Displaying a Procedure window

You can display a Procedure window from the tree view.

To display a Procedure window

1. Do one of the following:
   - Double-click on a procedure name in the tree view.
   - Double-click on an experiment object that uses the procedure.

   A Procedure window is displayed.

Displaying a Parameter Data window

You can display a Parameter Data window from the tree view.

To display a Parameter Data window

- Double-click on a parameter data set in the tree view.

  A Parameter Data window is displayed.

Using the list view

The list view can be used to:

- edit the name of an entry
- edit the description of an entry
- sort entries.



Refer to *"Using the tree view"*, p 11-8, for details about selecting an object and displaying Procedure and Parameter Data windows from the list view.

Expanding the list view

You can display the contents of a folder in the list view.



To expand a folder in the list view

- In the list view, move the cursor over the folder that you wish to expand, and double-click the **left** mouse button.

  The contents of the selected folder are displayed in the list view, and the tree view is updated to ensure that the selected folder is visible.

Editing an entry

You can edit the name of an object in the list view, or change its description.



To edit the name of an object

1. Select the entry in the list view that you wish to change.
2. Choose **File | Rename**. The object name is highlighted.
3. Enter the new name.

To edit the description of an object

1. Select the entry in the list view that you wish to change.
2. Choose **File | Properties** to display the Properties dialog box.
3. Enter the new description in the **Description** text box.
4. Select **OK** to confirm the changes, and to close the dialog box.

Sorting entries

You can sort the entries in the list view into ascending or descending alphabetical order.

To sort the entries in the list view

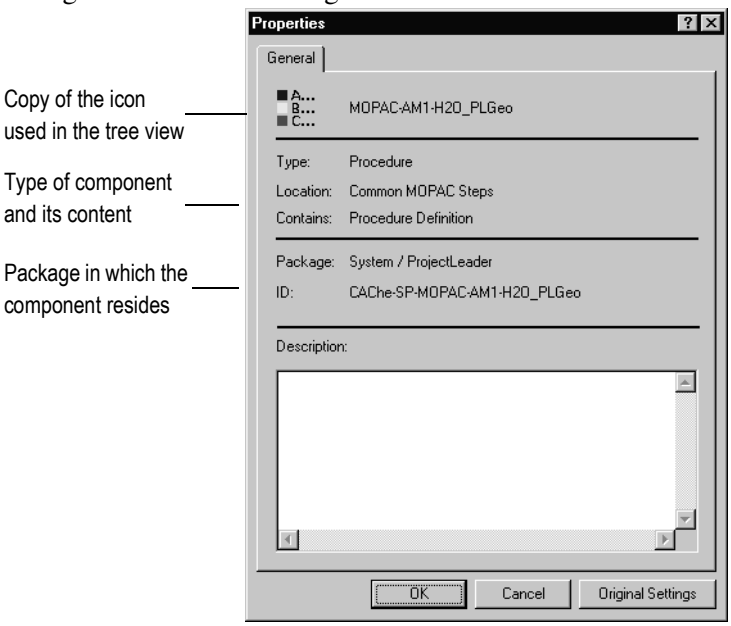
1. Choose one of the following:
   - **View | List Icons | by Name**
   - **View | List Icons | by Description**.

   Entries are sorted into ascending alphabetical order.

Showing properties of a component

You can select an environment component in the tree view or list view of the Navigator window and display its properties in a Properties dialog box.

The appearance of the Properties dialog box varies for each type of environment component. However the **General** tab of the Properties dialog box has the following common features:



Some properties can be edited to allow you to modify the properties of a particular environment component.

To display the properties of a component

1. In the tree view of the Navigator window, select an environment component.
2. Choose **File | Properties**.

   The Properties dialog box is displayed.

Available properties

Different properties are available for each type of environment component.Each different type of property is displayed on a different tab of the Property dialog box.

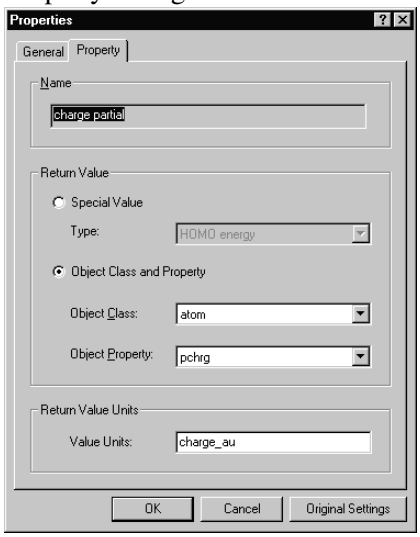
Experiment environment properties

You cannot edit the attributes of the **General** tab for the experiment environment component. You can edit the **Packages** tab to specify which packages to load when refreshing the experiment environment.

Refer to *"Refreshing the experiment environment"*, p 11-35, for full details of using the **Packages** tab to define which packages are loaded into the experiment environment.

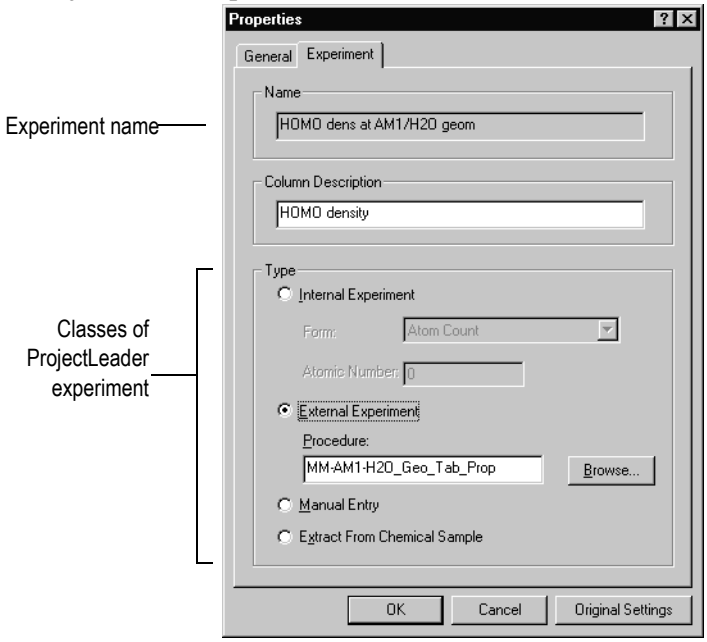
Property component properties

For Workspace property components the Property dialog box features a **General** tab. For ProjectLeader property components the Property dialog box also features a **Property** tab.



ProjectLeader experiment component properties

The ProjectLeader experiment component Properties dialog box contains an **Experiment** tab that allows you to select from the four classes of ProjectLeader experiment.



📖 NOTE The **Name** text box cannot be edited unless the dialog box is displayed when creating a new experiment.

The following parameters can be set for different types of internal experiment:

Experiment type	Parameters
Atom Count	Atomic number with available values in the range 0 to 102.
Bond Count	Bond order with available values of all, single, double, or triple.
Connectivity Index	Order with available values in the range 0 to 2. Normal or Polymer.
Group Count	Group type with available values of aldehyde or thio.
Ring Count	Ring size with available values of all rings, small rings, 5 membered, 6 membered, and large rings. Aromatic or non-aromatic.
Ring Size	Ring size with available values of smallest or largest.
Shape Index	Order with available values of 0 to 2. Normal or alpha-weighted.
Valence Connectivity Index	Order with available values of 0 to 2. Normal or Polymer.

The experiment types: Elemental analysis, Log P, Molar Refractivity, Molecular Formula, Molecular Weight, Net Charge, and Structure-Property Correlation have no additional controls.

Workspace experiment component properties

The Workspace experiment component Properties dialog box contains an **Experiment** tab that allows you to select the procedure associated with the experiment.

Modifying a procedure

A procedure is a named sequence of steps which are applied to one or more chemical samples. The procedure specifies the compute engine or engines used in the experiment.

You can modify a procedure by:

- adding or deleting steps
- rearranging the order in which the steps are performed
- changing the settings of the compute engine used.

A Procedure window allows you to modify the selected procedure. The Procedure window has five buttons that you can use:



The **New** button allows you to select new compute engine steps from a popup list.



The **Open** button allows you to view and change the settings for a selected compute engine step.



The **Delete** button allows you to remove the selected step from the procedure.



The **Up** button allows you to move a selected step nearer the beginning of the procedure. Each time the button is selected, the step is moved one step upwards.



The **Down** button allows you to move a selected step nearer the end of the procedure. Each time the button is selected, the step is moved one step downwards.

The **New** button can also be used to insert a new step that calls another procedure. This saves you having to duplicate all the steps of the second procedure within the one that you are modifying.

To modify a procedure

1. In the tree view of the Navigator window, select the procedure that you wish to modify.
2. Perform one of the following actions to display a Procedure window:
   - Press the **right** mouse button and choose **Open** from the popup menu.
   - Double-click on the selected procedure.

   The name of the procedure is displayed in the title bar of the Procedure window.
3. If required, you can:
   - add a step
   - call another procedure
   - move a step
   - view the settings of a step.

   Refer to the following sections for details about performing each of these actions.
4. If required, change the description of the procedure by typing into the **Description** text box.
5. When all the modifications have been made, choose **File | Close** to close the Procedure window.
6. Choose **File | Save** to save the modifications to the procedure.

NOTE You can import a step from a previous version of CAChe by using the **File | Import Step** option. Alternatively, you can drag setting files into the Procedure window.

Adding a step

You can add a step to a procedure.

To add a step

1. Select the step in the procedure after which you want to insert a new step.
2. Select the **New** button to display a popup menu.

   Alternatively, choose **File | New Step**.
3. Choose the name of the compute server that you wish to use.

   The selected step is added to the procedure, and the Settings dialog box, for the selected compute engine, is displayed.

Refer to *"Editing the settings of a compute engine"*, p 11-23, for details about editing these settings.

Deleting a step

You can delete a step from a procedure.

To delete a step

1. Select the step that you wish to remove.
2. Select the **Delete** button.

   The selected step is removed from the list of steps.

Moving a step

You can move a step from a procedure so that it appears nearer the beginning or end of a set of steps.

To move a step

1. Select the step that you wish to move.
2. Select the **Up** button to move the step upwards.

3. Select the **Down** button to move the step downwards.

   The selected step is moved up or down respectively.

Viewing the settings of a step

You can view the settings of a selected step.

To view the settings of a step

1. Select the step that you wish to view.
2. Select the **Open** button to display the Settings dialog box.

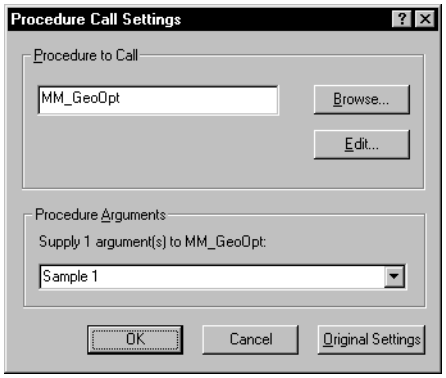
   Alternatively, choose **File | Edit Step**.

If you wish to change the settings of the compute engine used in an existing step, refer to *"Editing the settings of a compute engine"*, p 11-23.

Calling a procedure

You can call a procedure from within the procedure that you are modifying. The instruction to call the second procedure is added as a step within the procedure.

The Procedure Call Settings dialog box is used.



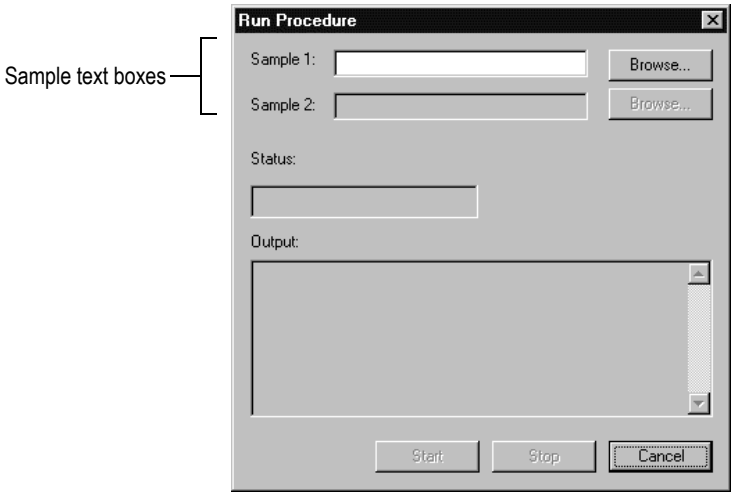
To call a procedure from another procedure

1. From the Procedure window, select the step in the procedure after which you want to insert the call to another procedure.
2. Select the **New** button to display a popup menu.
3. Choose **Procedure Call** to display the Procedure Call Settings dialog box.
4. Select the procedure that you wish to call from the **Procedure to Call** text box. Alternatively, you can select the **Browse** button and choose from the list of available procedures.
5. If required, change the procedure arguments in the **Procedure Arguments** drop-down list.
6. Select **OK** to confirm the procedure that you wish to call and to close the dialog box.

   A step calling the selected procedure is inserted into the list of steps.

Running a procedure

After modifying a procedure you can execute the procedure using the Run Procedure dialog box.



The dialog box features a **Sample n** text box, where **n** is the sample number, for each of the chemical samples used. For example, a procedure with two input arguments has a text box for Sample 1 and a text box for Sample 2.

The **Start** button is disabled until the location of all the samples has been specified. All output from the procedure is sent to the Output window.

The dialog box remains open until the procedure has completed or been aborted.

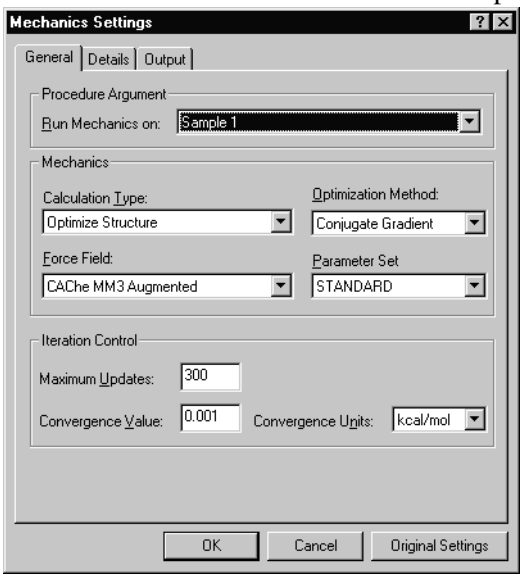
To run a procedure

1. In the tree view of the Navigator window, select the procedure that you wish to run.
2. Choose **Run | Procedure** to display the Run Procedure dialog box.
3. Specify the location of Sample 1 in the **Sample 1** text box.

   If you are unsure of the location, select the **Browse** button to display the Browse Procedures dialog box.
4. Repeat step three for any other required samples.
5. Select the **Start** button to run the procedure using the sample file(s) specified as input.

Editing the settings of a compute engine

You can edit the input arguments and settings for each of the compute engines available in CAChe. Each compute engine has a unique dialog box in which you can edit the settings. The dialog box for Mechanics is shown below as an example.



You can display the Settings dialog box for a compute engine from the Procedure window if:

- a new step is added to a procedure
- an existing step is viewed.

📖 NOTE Editing a compute engine step only changes the settings for the compute engine in the procedure featured in the Procedure window.

The inputs for each compute engine fall into three categories:

Arguments	This information is taken from the argument specified for the procedure in which the compute engine is used.
Settings	The control data for the compute engine.
Parameter data	The names of particular classes of parameter data, e.g., MM2 Standard.

To edit the settings of a new compute engine step

1. From the Procedure window, select the **New** button to display the Settings dialog box:

   For details about displaying the Procedure window, refer to *"Modifying a procedure"*, p 11-17.

2. Modify the settings for the compute engine, as required.

   Refer to the on-line Help system for CAChe for details of the settings available for each compute engine.

3. Select **OK** to save the changes to the compute engine.

   Alternatively, select **Original Settings** to return to the default machine settings for the compute engine.

NOTE You can remove user-defined settings from a compute engine step at any time by selecting the **Original Settings** button.

To edit the settings of an existing compute engine step

1. From the Procedure window, select the compute engine step that you wish to modify.

   For details about displaying the Procedure window, refer to *"Modifying a procedure"*, p 11-17.

2. Select the **View** button to display the Settings dialog box:
3. Modify the settings for the compute engine, as required.

   Refer to the on-line Help system for CAChe for details of the settings available for each compute engine.

4. Select **OK** to save the changes to the compute engine.

   Alternatively, select **Original Settings** to return to the default machine settings for the compute engine.

Refer to the CAChe on-line Help system for details about the settings available for each compute engine.

Creating experiments

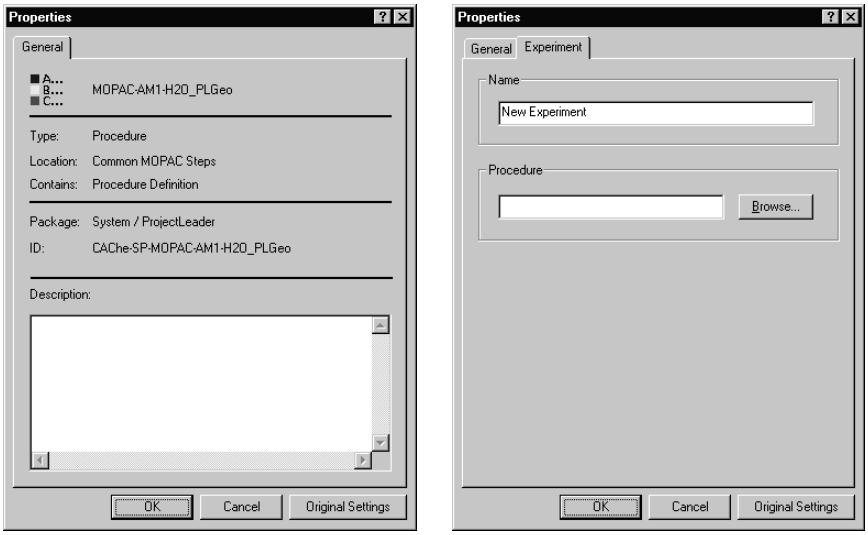
There are three ways to create an experiment using the Procedure Editor:

- create a new experiment from scratch
- clone an existing experiment and edit it
- import an existing CAChe experiment.

Creating a new experiment

You can create a new experiment in the Procedure Editor, and save it in the experiment environment.

Use the Properties dialog box to create a new experiment. This is a two tabbed dialog box which allows you to define a name, description, and procedure for the experiment.



You can choose the category of experiment property in which you want the new experiment to belong. Examples of categories of experiment property include partial charge and electrophilic susceptibility.

To create a new experiment

1. In the tree view of the Navigator window, select the class of experiment property in which you wish to include the new experiment.

   The new experiment will be placed in the folder that you select.

2. Perform one of the following actions to display the Properties dialog box:

   - Press the **right** mouse button and choose **New Experiment** from the drop-down menu.
   - Choose **File | New Experiment**.

3. In the **Experiment** tab, enter a name for the new experiment in the **Name** text box.

   By default the new experiment is called New Experiment.

4. Enter the name of the procedure that you wish the experiment to use in the **Procedure** text box. You may enter a name which does not currently exist.

   Alternatively, select the **Browse** button to select an existing procedure. The Browse Procedure dialog box is displayed. Select a procedure from the list and select **OK** to add the procedure to the Procedure text box.

5. Select the **General** tab of the Properties dialog box.

6. Enter a description of the new experiment in the **Description** text box.

7. Select **OK** to confirm the details of the new experiment, and to close the dialog box.

   The new experiment is added to the folder that you selected in step one.

8. If you entered the name of a procedure which does not exist, a Procedure window will be displayed to allow you to define it. Refer to *"Modifying a procedure"*, p 11-17, for details about defining a procedure.

9. Choose **File | Save** to save the changes to the experiment environment.

Cloning an existing experiment

You can create a new experiment by cloning an existing experiment and modifying its settings.

A copy of the selected experiment is placed at the same level as the original in the tree hierarchy. The procedure referenced within the experiment is also copied. The new experiment is assigned the same name as the original, with the suffix [2]. Similarly, the new procedure is assigned the same name as the original with the suffix [2]. The description text given to the new copy of the procedure is "Copy of <procedure>", where <procedure> is the name of the original procedure.

To clone an existing experiment

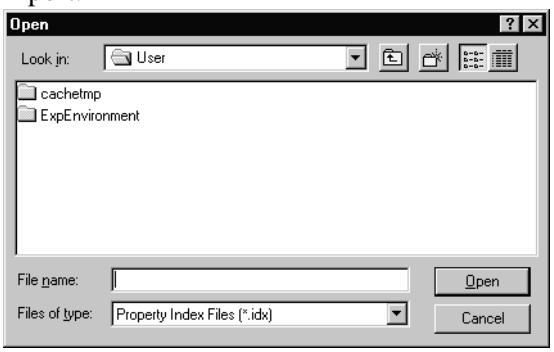
1. In the tree view of the Navigator window, select the experiment that you wish to clone.
2. Choose **Edit | Copy**.
3. Choose **Edit | Paste**.

Refer to steps two to eight of *"Creating a new experiment"*, p 11-25, for details about changing the settings of an experiment.

Importing a CAChe experiment

You can import an existing CAChe experiment into the experiment environment.

The Open dialog box is used to allow you to select an experiment to import.



You can import an experiment into the Workspace or ProjectLeader folder of the Navigator window.

You can also import procedures into the procedure index folder, and parameter data into the parameter data folder. To do this you should select the procedure index folder, or the parameter data folder respectively before using the **File | Import** command.

To import a CAChe experiment

1. In the tree view of the Navigator window, select one of the following folders:
   - select the Workspace folder if you want the experiment to be available in the Workspace
   - select the ProjectLeader folder if you want the experiment to be available in the ProjectLeader.
2. Choose **File | Import Experiments** to display the Open dialog box.

   Note that if you have not selected the Workspace or ProjectLeader folder this option will not be available.
3. Select the Property Index file that you wish to import and select the **Open** button to import the file.

This file contains the experiment.

The experiment is added to the tree view.



Refer to steps two to eight of *"Creating a new experiment"*, p 11-25, for details about changing the settings of an experiment

📖 NOTE The import facility always creates new environment components with unique names. The currently selected components are not overwritten.



Refer to *"Exporting environment components"*, p 11-37, for details about exporting experiments, procedures, and parameter data.

Expert modification

You can modify the parameter data of a compute engine. The modified parameter data is used for all experiments that use that compute engine with that set of parameter data.

A Parameter Data window is used to modify parameter data.

To modify parameter data

1. In the tree view of the Navigator window, move to the Parameter Data folder.
2. Double-click on the parameter data set that you wish to modify, e.g., the STANDARD set of MM2.

   A Parameter Data window is displayed.
3. Change any of the data in the window by selecting a value and overwriting with a new value.
4. When the modifications are complete, choose **File | Save** to save the modified parameter data set.

NOTE If you make any changes which are not satisfactory, choose **Edit | Original Settings** to revert to the system copy of the parameter data.

Creating a group procedure package

A package is a collection of different types of components that are used in the experiment environment. Examples of these components include the property and the sample used in an experiment.

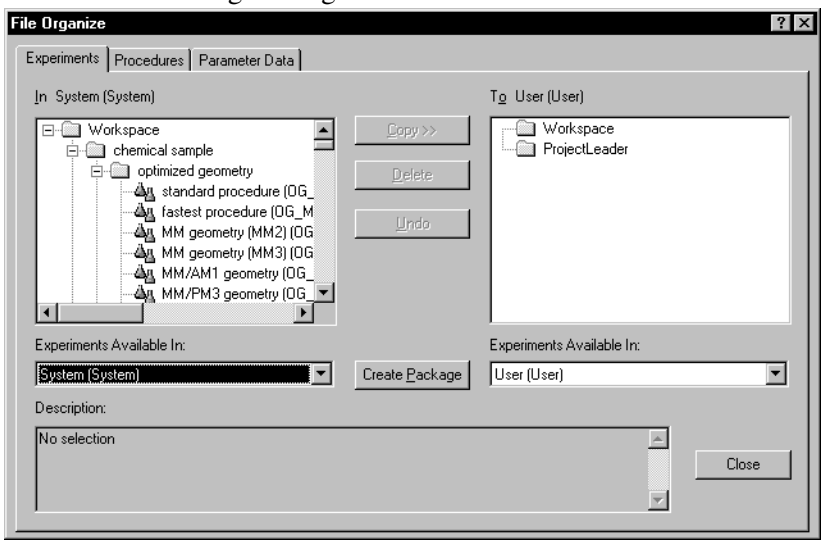
In the CAChe experiment environment there are three directories, each of which can contain packages:

System This directory relates to the location of the CAChe executables, and is shared by all users of the installation.

Group This directory contains packages that are available to a group of users. This feature is available to both multiple user installations of CAChe, and single user installations. In the case of single users, the group package(s) can be used to share CAChe experiments with other users.

User This directory contains packages available to a particular CAChe user.

You can create a new group procedure package for use by other users. Packages can be created from the Organizer dialog box using the Create Package dialog box.



This is a three-tabbed dialog box that allows you to copy files between user and group packages.

To create a group procedure package

1. Create experiments, procedure definitions, and parameter data as required in your own user package.

   Refer to *"Creating a new experiment"*, p 11-25, for details about creating an experiment.

   Refer to *"Modifying a procedure"*, p 11-17, for details about modifying a procedure.

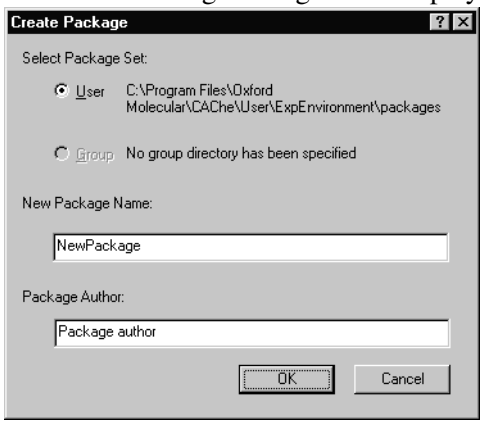
   Refer to *"Expert modification"*, p 11-30, for details about modifying a parameter data set.

2. Choose **File | Organizer**.

   The Organizer dialog box is displayed. This dialog box is displayed with an active tab which reflects the currently selected component in the tree view.

3. In the **Experiment** tab, select the **Create Package** button.

   The Create Package dialog box is displayed.



4. Select the **Group** radio button to specify that the new package should be available to group users.
5. Enter a name for the package in the **New Package Name** text box.
6. Enter the name of the author in the **Package Author** text box.
7. Select **OK** to create the package, and to close the dialog box.

8. To copy experiments into the Group package:
   - Select the **Experiment** tab of the Organizer dialog box.
   - Select the new group package from the right-hand **Experiments Available In** drop-down list.

     The new package is displayed in the **To Group** box.
   - From the **In User** box, select the components that you wish to copy to the new group package.
   - Select the **Copy** button to copy the selected components.
9. To copy procedures into the Group package:
   - Select the **Procedures** tab of the Organizer dialog box.
   - Select the new group package from the right-hand **Procedures Available In** drop-down list.

     The new package is displayed in the **To Group** box.
   - From the **In User** box, select the components that you wish to copy to the new group package.
   - Select the **Copy** button to copy the selected components.
10. To copy parameter data into the Group package:
    - Select the **Parameter Data** tab of the Organizer dialog box.
    - Select the new group package from the right-hand **Parameter Data Available In** drop-down list.

      The new package is displayed in the **To Group** box.
    - From the **In User** box, select the components that you wish to copy to the new group package.
    - Select the **Copy** button to copy the selected components.
11. When all the required components have been added to the new group package, select the **Close** button to close the Organizer dialog box.

Loading new packages

Once the group package has been created, all users who share the group package directory are informed of the availability of the new

package the next time they start the Procedure Editor, the Workspace, or the ProjectLeader.

The New Packages Available dialog box is displayed if the package set contains any new packages that were not present the last time the Procedure Editor, the Workspace, or the ProjectLeader was started.

You can select the packages that you wish to load.

📖 NOTE The New Packages Available dialog box will inform you in the future if any new packages are added to CAChe as a result of you or a System Administrator installing a new CAChe compute engine.

To select packages to be loaded

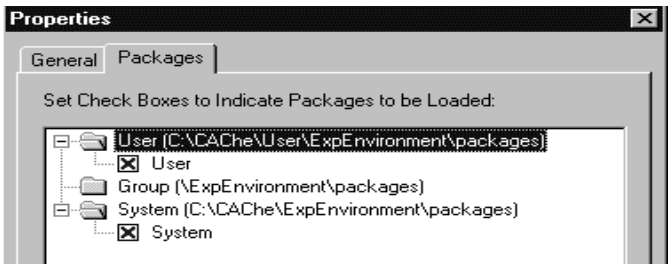
1. In the New Packages Available dialog box, select the packages that you wish to be loaded.
2. Select **OK** to confirm your selection and to close the dialog box.

📖 NOTE If you accept the default status by selecting the **OK** button without making any selection, then all packages will be loaded.

Refreshing the experiment environment

After creating or importing packages, you can refresh the experiment environment to include those new packages. Alternatively, you can specify any packages which you do not wish to include.

The **Packages** tab of the Property dialog box for the Experiment Environment component is used.



To refresh the experiment environment

1. In the tree view of the Navigator window, select the folder named **Environment**.
2. Choose **File | Properties** to display the Properties dialog box.
3. Select the **Packages** tab.

   All the available packages are shown with check boxes by each one.
4. To include a package, check the check box next to it.
5. To exclude a package, uncheck the check box next to it.
6. When you have made your selection, select the **Apply** button to refresh the experiment environment.

   The specified selection of packages is loaded.

Returning to original settings

You can select a component and revert it to its original definition. This action discards any overwritten version created by editing the component.

The original definitions for each component are stored in the System or Group directories. This action removes the modified definitions that reside in the User directory, exposing the originals in the System or Group directory.

To return to the original settings

1. In the tree view of the Navigator window, select the component that you wish to use.
2. Choose **Edit | Original Settings**.

   The component is reverted to its original settings.

NOTE Only definitions in the User directory can be overwritten.

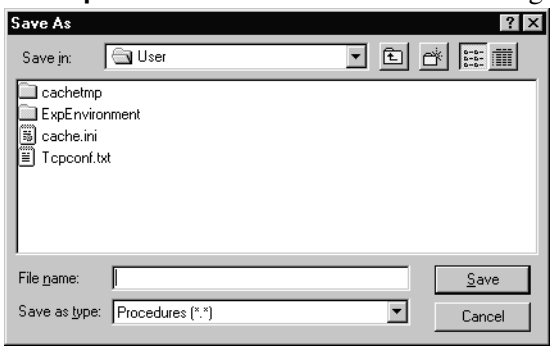
Exporting environment components

The following components can be exported:

- experiments
- procedures
- parameter data

The type of component which can be exported depends on the current selection in the tree view of the Navigator window.

The **Export** command uses the Save As dialog box.



To export an environment component

1. In the tree view of the Navigator window, select the component that you wish to export.
2. Choose **File | Export** to display the Save As dialog box.
3. Enter a name for the exported component in the **File Name** text box.
4. Select a directory for the component.
5. Select the **Save** button to export the component, and to close the dialog box.

Refer to *"Importing a CACche experiment"*, p 11-28, for details about importing environment components.

Quitting the Procedure Editor

To quit the Procedure Editor

1. Choose **File | Exit**.

   If you have any unsaved changes in the displayed experiment environment, an alert box asks if you would like to save changes.

2. Do one of the following:
   - Select **Yes** to save the changes and exit the Procedure Editor.
   - Select **No** to exit the Procedure Editor without saving the changes.
   - Select **Cancel** to keep the Procedure Editor running.

12 Using ProjectLeader

Overview

ProjectLeader is a component of CAChe that is used to automate the calculation of properties, and to perform analyses on multiple chemical samples.

This chapter describes how you can use ProjectLeader to:

- perform experiments on chemical samples, or on components of chemical samples such as atoms and bonds
- carry out statistical analyses and evaluate equations
- plot scatter plots of the results of experiments and analyses.

Refer to Chapter 10, *"Performing Workspace Experiments"*, for an overview of performing experiments in the CAChe workspace, and *"Workspace versus ProjectLeader"*, p 2-21, for a comparison.

Contents

Introduction to ProjectLeader 12-2
ProjectLeader experiments 12-3
Starting ProjectLeader 12-5
Using the ProjectLeader workbook 12-7
Opening a ProjectLeader project 12-11
Adding chemical samples 12-12
Using the CAChe Workspace from a worksheet 12-14
Copying objects from ChemDraw, ISIS Draw, or ChemFrontier 12-15
Viewing sample properties 12-17
Editing sample properties 12-18
Copying sample properties 12-18
Running a ProjectLeader experiment 12-20
Adding a chemical sample column, property, sample component, analysis, or comment to a worksheet 12-21
Selecting a server 12-24
Selecting cells 12-24
Evaluating the cells 12-25
Editing data 12-26
Using scatter plots 12-27
Changing workbook display options 12-33
Changing the chemical sample display 12-33
Sorting rows 12-34
Changing the grid line display 12-35
Changing the text display 12-36
Changing the numerical display 12-36
Hiding and displaying worksheet features 12-37
Using worksheet footnotes 12-37
Viewing cell information 12-39
Printing files 12-40
Previewing a printout 12-40
Choosing print options 12-40
Printing a ProjectLeader window 12-42
Exporting a ProjectLeader worksheet 12-43
Saving a ProjectLeader project 12-44
Quitting ProjectLeader 12-45

Introduction to ProjectLeader

ProjectLeader is a separate application from the CAChe Workspace. ProjectLeader simplifies the application of computer-aided chemistry by letting you specify first the chemical property that you want evaluated, then the procedure for evaluating that property. By contrast, CAChe Workspace requires you to choose the procedure, then select the property to be evaluated..

📖 NOTE ProjectLeader is not part of BioCAChe, Personal CAChe, Quantum or *Ab Initio* CAChe.

ProjectLeader offers the ability to perform calculations on several chemical samples at the same time. A wide range of experiments is available, including experiments similar to those you can perform in the Workspace, plus experiments not available in the Workspace such as calculating connectivity indexes, dipole vectors, and the octanol-water partition coefficient.

Experiments may be performed on entire chemical samples, or on chemical sample components such as atoms, bonds, and molecular orbitals.

Refer to *"ProjectLeader experiments"*, p 12-3, for a full list of the experiments available in ProjectLeader.

Viewing and analyzing columns of experimental data for several chemical samples at once enables you to establish mathematical relationships between one set of data and another, thus aiding:

- the process of calibration by comparing the results of measurements on specific instruments with the known standard results
- the calculation of quantitative structure activity relationships (QSAR) between molecular structure and pharmacological activity, and quantitative structure property relationships (QSPR) between molecular structure and properties such as boiling points, octanol-water partition coefficients, and dipole moments.

Once you have performed several experiments and analyses, you may wish to plot a scatter plot of the results. The straight line fitting in ProjectLeader's scatter plots provides a powerful way of identifying trends in your results.

ProjectLeader experiments

The following list includes some of the experiments that are available with ProjectLeader. These experiments can be performed on one or more chemical samples simultaneously:

- optimization to find a low energy structure for steric energy, heat of formation, or total energy
- net positive and negative charge for a molecule
- molecular formula, weight, and refractivity
- ring count and size
- investigation of molecular orbital energies such as HOMO and LUMO energies
- calculation of the dielectric, steric, total energy, and heat of formation of a structure at its current geometry
- investigation of visible and UV-visible spectra data
- zero-order, first-order, and second-order molecular or valence connectivity indices
- dipole moment and dipole vectors x, y, and z
- electron affinity
- shape index order 1, 2, and 3
- octanol-water partition coefficient.

Experiments can also be performed on sample components, such as atoms, bonds, and molecular orbitals.

ProjectLeader supports the statistical analyses of chemical samples, such as multiple linear regression, forward and reverse stepwise regression, and calculations based on customizable equations.

ProjectLeader experiments use the same set of computational applications as Workspace experiments.



Refer to Chapter 20, *"CACheComputational Applications"*, for further details.

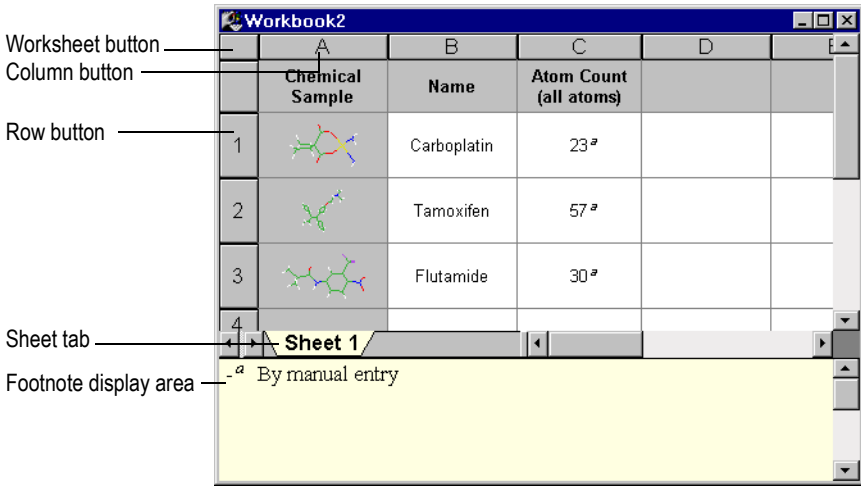
Starting ProjectLeader

To start ProjectLeader

1. Do one of the following:
   - Choose **Start** | **Programs** | **CAChe** | **ProjectLeader** from the Windows taskbar.
   - In Windows Explorer, double-click the **plwin.exe** icon in the `CAChe` folder.

   The splashscreen is displayed.

   After a few seconds an empty ProjectLeader workbook, `Untitled1`, is opened.



Column, row, and worksheet buttons

Each column has a lettered column button, and each row has a numbered row button. Click on these to select a whole column or row respectively. Click on the worksheet button to select the whole worksheet.

Sheet tab

Each worksheet in a workbook has a sheet tab. Click on the sheet tab to make the worksheet active. Sheet tabs can be renamed, Refer to *"Worksheets"*, p 12-9 for further details.

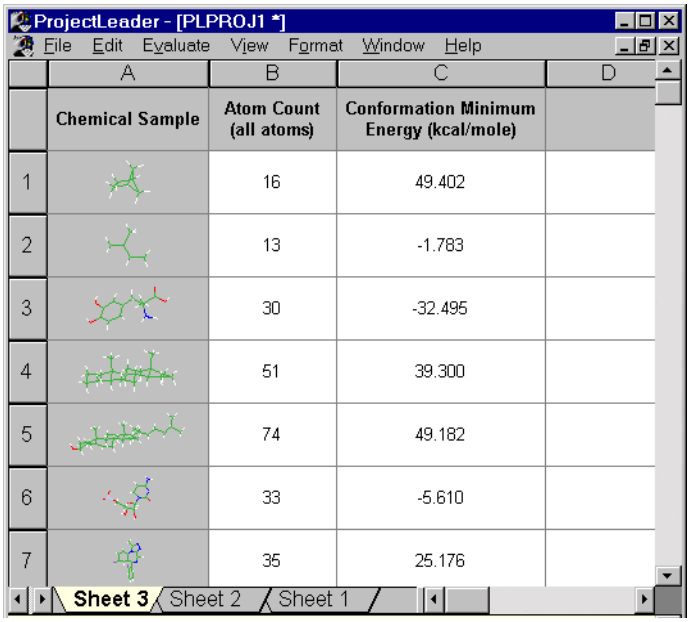
Footnotes

Footnotes can be defined for each worksheet cell. They are displayed in the footnote display area, underneath the ProjectLeader worksheet.

Using the ProjectLeader workbook

When you start ProjectLeader, an empty workbook is displayed. The following illustration shows a ProjectLeader workbook to which the following have been added:

- Chemical Sample files (displayed as line drawings here)
- experiments investigating molecular properties
- experimental results contained in the relevant worksheet cells
- worksheets.



NOTE The modification state of a project is indicated by a * attached to the title of each project window.

The Chemical Sample column

The first column in the worksheet is the Chemical Sample column. When you add chemical samples to ProjectLeader they are displayed in this column.

You can also open the CAChe Workspace from the Chemical Sample column, in order to:

- view an existing chemical sample contained in the worksheet
- create a new chemical sample to add to the worksheet.

The column title row

The first row in the worksheet is the column title row. The column titles are displayed underneath alphabetically-labeled column buttons. The property or analysis that you want to calculate is added to the column title cells.

Worksheet cells

Experiments and analyses are performed by evaluating worksheet cells. The experiment or analysis is defined by the chemical sample in the Chemical Sample column, and the experiment or analysis in the column title row.

Worksheet cells display the status of calculations as they are performed, then display the results when experiments are complete.

Refer to *"Running a ProjectLeader experiment"*, p 12-20, for more information.

Mouse actions in ProjectLeader

Most tasks in ProjectLeader can be accomplished by using mouse actions.

Double-click on a cell in the Chemical Sample column or the column title row to open a dialog box that lets you define information for that cell. Double-click on a cell in:

- the Chemical Sample column to open a sample in that cell

- the column title row to define the type of information to be displayed in that column: a property, an analysis, or a comment.

Right mouse click on a cell in the ProjectLeader worksheet to display a pop-up menu listing actions that can be performed for that cell.

A different pop-up menu is displayed if you click the right mouse button on a sheet tab in the ProjectLeader workbook, on a cell in the Sample Properties workbook, and yet another from a right mouse click on a scatter plot.

Worksheets

Each workbook can contain many worksheets. Select the sheet tabs to move from one worksheet to another.

ProjectLeader enables you to:

- insert a sheet
- delete a sheet
- rename a sheet
- move a sheet.

To insert a sheet

- Choose **Edit | Insert Sheet**.

  A new sheet is inserted to the immediate left of the currently selected sheet.

To delete a sheet

1. Select the sheet tab that you want to delete.
2. Choose **Edit | Delete Sheet**.

   The sheet is deleted from the workbook.

To rename a sheet

1. Select the sheet tab that you want to rename.

2. Choose **Edit | Rename Sheet**.
3. Enter a new name in the Rename Sheet dialog box, and select **OK**.

   The sheet is renamed.

To move a sheet

1. Select the sheet that you want to move.
2. Choose **Edit | Move Sheet** to display the Move Sheets dialog box.
3. As required, select either:
   - **Move Up**
   - **Move Down**
4. Select **OK** when the sheet has been reordered to your requirements.

TIP Select a sheet tab using the **right** mouse button to display a pop-up menu listing the commands for managing worksheets.

Opening a ProjectLeader project

ProjectLeader projects can be saved as project files so that you can continue working on a project at a later time. ProjectLeader project files are saved with the extension `.plp`.

To open an existing ProjectLeader project

1. Choose **File** | **Open** to display a dialog box.
2. Move to the directory that contains the project that you want to open.

   The files are filtered so that only files that have the extension `.plp` are displayed.
3. Select the project that you want to open.
4. Select **Open**.

   The project is opened in a ProjectLeader workbook.

Adding chemical samples

Chemical samples can be added to the ProjectLeader worksheet from:

- CAChe Chemical Sample files (`*.csf` files)
- MDL SD files (`*.sd`, `*.sdf` files)
- MDL MOL files (`*.mol` files).

Multiple files of each format can be added simultaneously.

Chemical samples can be added straight to ProjectLeader from file. Alternatively, you can open the Workspace from the worksheet, draw a new Chemical Sample file, save it, then add the new file to the worksheet.

To add existing files

1. Double-click on a cell in the Chemical Sample column to display the Open dialog box.
2. From the **Files of type** drop-down list, choose the format of the files that you want to import.
3. Select the files that you want to import.

   You can add multiple Chemical Sample files, or multiple SD and MOL files, but you cannot import a mixture of Chemical Sample files and SD or MOL files simultaneously.
4. Hold down **Shift** and select the first and last files in a group to select all of the files in that group. Hold down **Ctrl** and select more files to add single files to the selection.

   In order to display multiple chemical samples, ProjectLeader will insert new rows directly below the cell that you have selected.
5. Select **Open**.
   - If you are importing Chemical Sample files or MOL files, the structures are displayed in the Chemical Sample column, and the process of adding the files is complete.
   - If you are importing SD files, the Import an MDL SD File

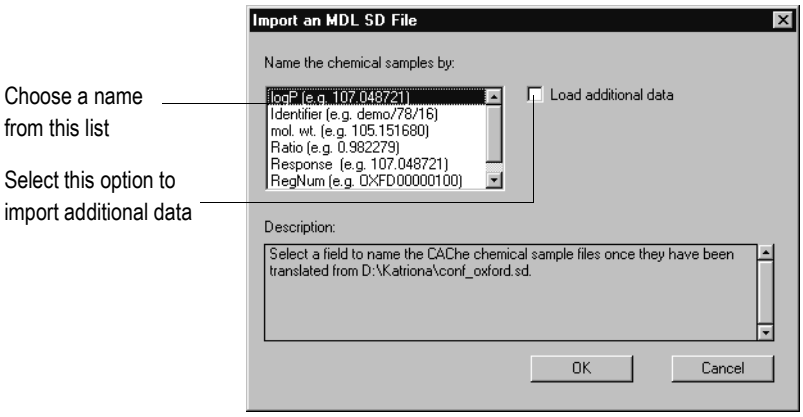
dialog box is displayed. Continue with steps 6 through 8, below, to complete the process.

CACHe reads SD or MOL files and translates them to CACHe Chemical Sample files, one chemical sample per file. Because multiple chemical samples can be contained in one SD file, and only one chemical sample can be saved in each CACHe Chemical Sample file, you are prompted to define the way in which you want to name the new Chemical Sample files.

6. In the Import an MDL SD file dialog box, choose a name from the scrolling list of possible names for the chemical samples.
7. Select the **Load additional data** radio button if you want to import any data from the SD file other than the structures.

   Additional data will be loaded in the first unoccupied columns.
8. Select **OK**.

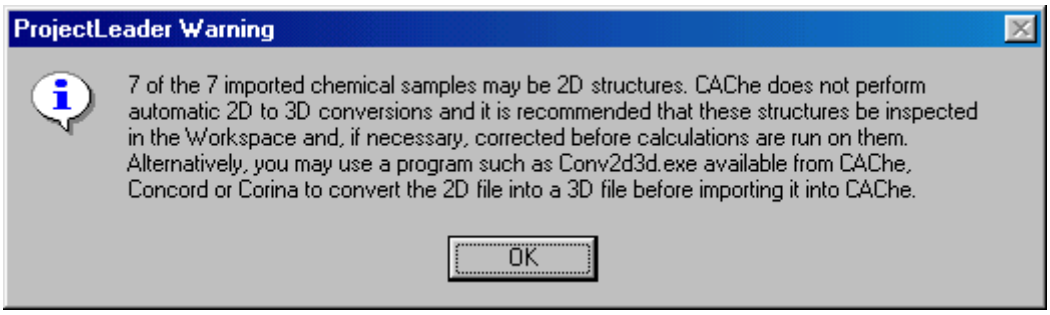
   The structures are displayed in the Chemical Sample column.



The name of each sample is saved with the worksheet cell.

CACHe works primarily with 3D structures. Many corporate databases contain only 2D chemical structures. The 2D structures must be converted to 3D before performing experiments that require 3D coordinates. If your SD file appears to contain 2D coordinates instead of 3D coordinates, you will

receive this informational message:



When a Chemical Sample file is added to a worksheet, you have the option to display it either as a line drawing or by name. Line drawings are displayed by default, and have the advantage that you can enlarge them in order to view the details more clearly.

Refer to *"Changing workbook display options"*, p 12-33, for details of changing the chemical sample display.

Using the CAChe Workspace from a worksheet

ProjectLeader allows you to view a chemical sample in the CAChe Workspace by selecting the sample from a ProjectLeader worksheet. You can also open the Workspace and create a new Chemical Sample file.

Displaying the CAChe Workspace

To open an existing Chemical Sample file in the Workspace

1. Hold down **Shift** and click on a chemical sample in the ProjectLeader worksheet.

   The Workspace is opened, displaying the selected Chemical Sample file. The selected worksheet cell in ProjectLeader is colored pink to indicate that the corresponding Chemical Sample file is currently displayed in the Workspace.

2. Edit the chemical sample in the Workspace and save the file.

   The changes are displayed in the worksheet cell in

ProjectLeader.

To add a new Chemical Sample file to a ProjectLeader worksheet

1. Hold down **Shift** and click on an empty cell in the Chemical Sample column.

   The CAChe Workspace is opened, displaying a new, empty Chemical Sample file.

   The selected worksheet cell is colored pink to indicate that it is linked to the Chemical Sample file that is currently displayed in the Workspace.

2. Draw a molecule and save the Chemical Sample file.

   The chemical sample is displayed in the relevant ProjectLeader worksheet cell.

Refer to Chapter 4, *"Creating Chemical Samples"*, for details about drawing and saving the molecule.

Copying objects from ChemDraw, ISIS Draw, or ChemFrontier

You can copy any selected object to the Windows Clipboard from ChemDraw, ISIS Draw or ChemFrontier, and paste it into a ProjectLeader worksheet. Likewise, you can copy an object to the Windows Clipboard from a ProjectLeader worksheet, in MDL format, and paste it into one of these programs.

To copy and paste an object from ChemDraw, ISIS Draw or ChemFrontier

1. Select the object that you want to copy by clicking on it with a selection tool.
2. Do one of the following:
   - choose **Edit | Copy**
   - press **Ctrl C**.
3. Select an empty cell in the Chemical Sample column in which to paste the object.

4. Do one of the following:
   - choose **Edit** | **Paste**
   - press **Ctrl V**.

   The **Save As** dialog box is displayed.
5. Enter a name for the file, and select **Save**.

   A copy of the selected object is pasted in the cell.

   The copied object remains on the Windows Clipboard until you copy or cut another object, so you can continue to paste copies of the object until you have the required number of copies.

Viewing sample properties

ProjectLeader's main workbook is used to display chemical samples and the results of experiments and statistical analyses.

In addition to ProjectLeader's main workbook, you can open the Sample Properties workbook to view information about the following components of the chemical samples:

atoms	bonds
orbitals	molecule groups
electronic spectra	vibrational spectra
improper torsion angles	crystals
bond angles	dihedral angles
atom distances	molecular orbitals
Slater-type orbital basis functions	Gaussian-type orbital basis functions

Each component is displayed on a different sheet in the workbook.

📖 NOTE Sample properties can only be viewed if the information is available in the Chemical Sample file.

Experiments can be performed on the sample properties in the Sample Properties workbook in the same way as in the ProjectLeader workbook. Information can also be copied into the ProjectLeader workbook, where further experiments can be performed.

To view the sample properties

1. Select the chemical sample that you are interested in.
2. To display the Sample Properties workbook, do one of the following:
   - choose **View | Sample Properties**
   - click the **right** mouse button to display a popup menu and choose **View Sample Properties**.
3. Select the tabs at the bottom of the workbook to view information about the different components.

Refer to *"Running a ProjectLeader experiment"*, p 12-20, for details of performing experiments in the Sample Properties workbook.

Editing sample properties

By default, the Sample Properties workbook is locked against editing. However, it is possible to unlock it, and to edit the values in the workbook.

NOTE Care should be taken when editing sample properties, because ProjectLeader does not check the validity of any changes made to chemical samples.

To edit a sample property

1. Choose **Edit | Edit Property Values**.

   The lock icon is removed from the Sample Properties workbook.

2. Edit the cells that you want to change.

   Cells that have been edited automatically have a footnote added to them, warning you that the cell has been edited.

3. Choose **Edit | Lock Property Values** to lock the sample properties again.

   This avoids the risk of editing properties accidently.

Copying sample properties

Sample properties can be copied to the ProjectLeader workbook and displayed in the same row as the chemical sample to which they relate. Experiments can then be performed on the sample properties in the ProjectLeader workbook.

To copy sample properties to the ProjectLeader workbook

1. In the Sample Properties workbook, select the cells that you want to copy to the ProjectLeader workbook.
2. To display the Select Columns dialog box, do one of the

following:

- choose **Edit | Copy to Main Workbook**
- click the **right** mouse button to display a popup menu and choose **Copy to Main Workbook**.

It prompts you to choose the first column in the ProjectLeader workbook to which the sample property data should be copied.

3. In the Select Columns dialog box, choose the first column to which the cells should be copied.

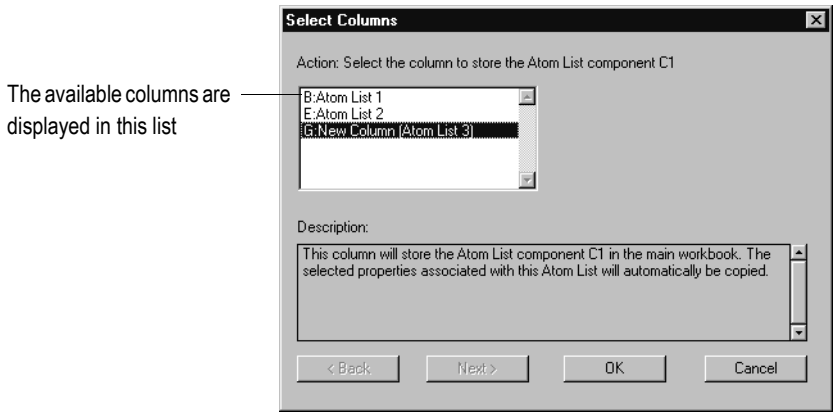
   You must choose a column in the ProjectLeader workbook for each of the rows in the Sample Properties workbook from which you are copying data.

4. If you are copying data from more than one row in the Sample Properties workbook, select **Next**, then choose a ProjectLeader workbook column for the next row of data, until you have chosen a column for each of the rows.

5. Select **OK**.

   The cells are copied into the ProjectLeader workbook.

Refer to *"Running a ProjectLeader experiment"*, p 12-20, for details about performing experiments on sample properties when they are in the main ProjectLeader workbook.



Running a ProjectLeader experiment

A ProjectLeader experiment can be the calculation of a property, or the calculation of an analysis.

ProjectLeader experiments can be run on entire chemical samples or on components of chemical samples. Experiments can be run from the ProjectLeader workbook, or from the Sample Properties workbook.

Refer to *"Viewing sample properties"*, p 12-17, for details of viewing sample properties and copying the information into the ProjectLeader workbook.

To run a ProjectLeader experiment on one or more chemical samples or sample components, you use the following steps:

1. Add a chemical sample column, property, sample component, analysis, or comment to a worksheet.

Refer to *"Adding a chemical sample column, property, sample component, analysis, or comment to a worksheet"*, p 12-21

2. Select a server on which to run the experiment.

Refer to *"Selecting a server"*, p 12-24

3. Select the cells on which you want to experiment.

Refer to *"Selecting cells"*, p 12-24

4. Evaluate the cells.

Refer to *"Evaluating the cells"*, p 12-25

NOTE Before performing an experiment to calculate polymer properties, you must open the chemical sample in the Workspace, select the terminal carbon and hydrogen atoms of the polymer, and save the Chemical Sample file.

Adding a chemical sample column, property, sample component, analysis, or comment to a worksheet

ProjectLeader experiments are defined by assigning a property, sample component, or analysis to a worksheet column, then evaluating the cells in that column. The chemical sample information for the row provides ProjectLeader with enough information to evaluate the cells.

If no column is appropriate to provide information for the property of a sample component, a new column containing an appropriate sample component is automatically inserted.

You can add Chemical Sample columns to a ProjectLeader worksheet in addition to the Chemical Sample column that represents the first column in a worksheet. This enables you to compare the results of calculations between different columns of chemical samples.

To add a chemical sample column

1. Double-click on an empty column title cell to display the Enter Property dialog box.
2. Select the **Chemical Sample** radio button.
3. Select **OK**.

   The column title cell is labeled Chemical Sample, and chemical samples can be added to the column.

To add a property to a worksheet

1. Double-click on an empty column title cell to display the Enter Property dialog box.
2. Select the **Property of** radio button.
3. Select an option from the **Property of** drop-down list, then select **Next**.

   The available properties are displayed in a scrolling list. A brief description of the selected property is displayed underneath the list. Selecting a property displays its description.
4. Select a property to investigate from the **Kind of property**

scrolling list, then select **Next**.

5. Select a procedure from the **Kind of procedure** scrolling list.
6. If required, choose **Edit** to edit the procedure.

   The Procedure Editor is opened. Refer to Chapter 11, *"Using the Procedure Editor"*, for information on the Procedure Editor.
7. Select **OK**.

   If you have more than one Chemical Sample column in a worksheet, you will be prompted to select a column.
8. From the Column Select dialog box, do one of the following:
   - select a column from the list and choose **OK** to perform the calculation on that column
   - select **Automatic** to perform the calculation on the Chemical Sample column to the nearest left of the new column.

   The property is displayed in the column title cell at the top of the relevant column. When you evaluate any cell in this column, the chosen property is calculated.

TIP To undo a command, choose **Edit | Undo**.

To add a sample component to a worksheet

1. Double-click on an empty column title cell to display the Enter Property dialog box.
2. Select the **Sample Component** radio button, then select **Next**.
3. Select an option from the **Kind of sample component** drop-down list, then select **Next**.
4. Select a procedure from the **Kind of procedure** scrolling list.
5. Select **OK**.

   If you have more than one Chemical Sample column in a worksheet, you will be prompted to select a column.
6. From the Column Select dialog box, do one of the following:
   - select a column from the list and choose **OK** to perform the calculation on that column
   - select **Automatic** to perform the calculation on the Chemical Sample column to the nearest left of the new column.

The sample component is displayed in the column title cell at the top of the relevant column. When you evaluate any cell in this column, the chosen sample component is calculated.

To add a statistical analysis to a worksheet

1. Double-click on an empty column title cell to display the Enter Property dialog box.
2. Select the **Analysis** radio button, then select **Next**.
3. Select one of the types of regression from the **Kind of analysis** scrolling list, then select **Next**.
4. Select the column that contains the data you want to predict from the **Predict** scrolling list.
5. Select one or more columns to include in the regression from the **Using** scrolling list.
6. Select **OK**.

   The regression equation, regression coefficient and cross-validation are given in the column title. When you evaluate any cell in this column, the regression is evaluated. Columns with no predictive power, that is those without any variance, are omitted from the regression. The regression equation for each cross-validation step can be distinctly different for each model, even if the overall regression equation is the same for a given set of data to predict one variable.

To add an equation to a worksheet

1. Double-click on an empty column title cell to display the Enter Property dialog box.
2. Select the **Analysis** radio button, then select **Next**.
3. Select **Algebraic Equation**, then select **Next**.
4. Type an algebraic equation into the **Equation** panel.

   Start the equation with an equals sign, and use letters to refer to the worksheet columns.
5. Select **OK**.

   The equation is displayed in the column title cell at the top of the

column.When you evaluate any cell in this column, the chosen equation is evaluated.

To add a comment to a worksheet

1. Double-click on an empty column title cell to display the Enter Property dialog box.
2. Select the **Comment** radio button, then select **Next**.
3. Type the title for the column in the **Comment** panel, then select **OK**.

   The title is displayed in the column title cell at the top of the relevant column. Edit the cells individually to add comments.

Selecting a server

To select a server on which to run the experiment

1. Choose **Evaluate** | **Select Server** to display the Select Server dialog box.
2. Select a server by clicking on it, then select **OK**.

TIP You can find out which server is currently selected by choosing **Evaluate** | **Show Server**.

Selecting cells

To select cells

1. Select one or more cells to include in the experiment, where the row of the cell corresponds to the chemical sample on which you want to experiment, and the column of the cell corresponds to the property or analysis that you want to investigate or perform. Use one of the following to select the cells:
   - To select a group of adjacent cells, click and drag the mouse over the cells.
   - To select one or more non-adjacent cells, hold down the **Ctrl** key and click on the cells.

- To select a whole column, click on the relevant lettered column button.
- To select a whole row, click on the relevant numbered row button.
- To select the whole worksheet, click on the worksheet button, or choose **Edit | Select All**.

The cells are highlighted in black to show that they are selected.

Evaluating the cells

To evaluate the selected cells

1. To evaluate selected cells, do one of the following:
   - choose **Evaluate | Cell**
   - press the **right** mouse button and choose **Evaluate Cell** from the popup menu.

   Individual cells display the status of the calculations being performed, then the results as calculations are completed.

TIP You can stop a lengthy evaluation by choosing **Evaluate | Stop Cell Evaluation**.

Parallel cell evaluation

Where two or more columns of cells are to be evaluated, ProjectLeader checks to see whether the individual cell evaluations correspond to the same named procedure, running on the same chemical sample. If so, the experiment is run only once so that analyses are calculated on the same chemical state of the chemical sample.

Editing data

You can cut, copy and paste selected data in ProjectLeader, and you can insert or delete selected columns or rows.

The following actions can be chosen from the Edit menu:

Cut	to remove selected cells from the worksheet.
Copy	to copy selected cells to the Windows Clipboard.
Paste	to insert copied data into selected cells. Any existing data in the cells is overwritten.
Clear	to clear the data in selected cells.
Delete	to delete selected columns or rows from the worksheet. Any adjacent columns or rows in the worksheet move correspondingly.
Insert	to insert columns or rows before the selected column or row. Any adjacent columns or rows move correspondingly.

📖 NOTE If you attempt to delete cells in a ProjectLeader worksheet that provide the source of information for other cells, a warning will be displayed. For example, deleting a sample component column in a worksheet, where a property of sample component column exists, will disallow you from evaluating the cells in the property of sample component column.

Using scatter plots

Scatter plots enable you to view trends in data columns.

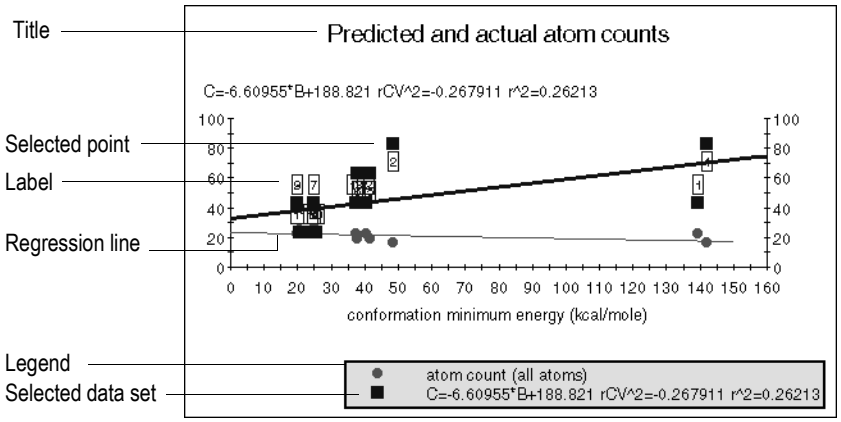
To plot a scatter plot

1. Select the data columns that you want to plot as a scatter plot.
2. Choose **View** | **Scatter Plot** to display a dialog box that prompts you to choose the columns for each axis of the scatter plot.

   You can have one column of data plotted along the horizontal axis, and multiple columns along the vertical axis.

   By default, the first column that you chose from a ProjectLeader worksheet is assigned to the horizontal axis, and the other columns are assigned to the vertical axis. If only one column is selected, it is assigned to the vertical axis.
3. Specify the columns that you want to plot on each axis.
4. Select **OK** to plot the scatter plot.

   The scatter plot is displayed so that it is the same size as the worksheet from which it was plotted.
5. Click and drag a corner of the scatter plot window to resize it.



Changing the display of the plot

To scale the plot

1. Hold down **Ctrl**, the **left** mouse button, and the **right** mouse button, then do one of the following:
   - drag the cursor **up** and to the **left** to make the plot smaller
   - drag the cursor **down** and to the **right** to make the plot larger.
2. To zoom in on a particular part of the plot, hold down **Ctrl** and the **left** mouse button, and drag the cursor over the area that you want to zoom in on.

   A rectangular box is drawn around the section, then the display is zoomed in on that section.
3. To reset the view, choose **View | Reset graph**.

To translate the plot

1. Hold down **Shift**, the **left** mouse button, and the **right** mouse button, then drag the cursor in the direction that you want to translate the graph.
2. To reset the view, choose **View | Reset graph**.

Selecting data points

You can select single data points, entire data sets, or combinations of points. Menu actions apply to all selected data points.

To select data points

1. Use the **left** mouse button to select a single data point.

   The label of the selected data point is boxed to indicate that the point is selected.
2. Use the **right** mouse button to display the popup menu for the selected data point.

   The menu options are activated, but only relate to the selected point. **Regression** is still grayed out, because an entire data set must be selected before a regression analysis can be performed.

3. To select an entire data set, select a data set from the legend.

   All of the data points in the data set are highlighted and the name of the data set is displayed on the vertical axis.

4. Use the **right** mouse button to display the popup menu for any highlighted data point.

   The menu options for any highlighted data point now relate to all of the highlighted data points.

To toggle the selection of data points

- Hold down **Ctrl** and select the **left** mouse button to toggle the selection of the selected points.

All data points that were selected become unselected, and data points that were unselected become selected.

Changing the labeling of the points

To label data points

1. To select the data points that you want to label, do one of the following:
   - select an individual point to label one point only
   - select a data set to label an entire data set.
2. Click the **right** mouse button to display the popup menu, and choose one of the following menu options:

Number	The number of the point. Points are numbered in the order that they appear in the worksheet.
Name	The name of the sample and the number of the point.
X-Value	The x-value of the point.
Y-Value	The y-value of the point.
Value Pairs	The x- and y-values of the points.
None	No label.

The chosen label is displayed next to the selected points.

Changing the title of the plot

To change the title of the plot

1. Double-click on the title of the plot to display the Graph Title dialog box.
2. Edit the text box as required.
3. Select **OK** to update the title.

NOTE Deleting all of the text of the title is equivalent to removing the title.

To hide the title of the plot

- Choose **View | Title** to toggle off the display of the title.

The title of the plot is hidden.

Changing the legend of the plot

To change the legend of the plot

1. Double-click on the legend of the plot.
2. Edit the legend as required.

To hide the legend of the plot

- Choose **View | Legend** to toggle off the display of the legend.

The legend of the plot is hidden.

Changing the axes labels

To change the axes labels

1. Double-click on an axis label.
2. Edit the axis label as required.

Hiding the footer of the plot

To hide the Footer of the plot

- Choose **View | Footer** to toggle off the display of the footer.

The footer of the plot is hidden.

Fitting a straight line

Regression analysis gives a best-fit straight line for one of the data sets, and the regression equation between that data set and the data set plotted on the X axis. The r^2 value gives the correlation of the data.

To fit a straight line

1. Select the data set to which you want to fit a line.
2. Place the mouse cursor anywhere in the scatter plot and click the **right** mouse button.

   A popup menu is displayed.
3. Choose **Regression** from the menu.

   The best-fit line is drawn through the results of the regression analysis, and the regression equation is given underneath the scatter plot.

Exporting the plot

To copy the plot to another application

1. Select the scatter plot that you want to copy, then choose **Edit | Copy**.
2. Switch to another application, and choose **Edit | Paste** to paste an image of the plot.

Printing the plot

To print the plot

- Select the scatter plot that you want to print, then choose **File | Print**.

Closing the plot

If a ProjectLeader project is closed while scatter plot windows are open, the plots are saved to the project file. When the project is reopened, the scatter plot windows are redisplayed.

Changing workbook display options

You can change the display of the following items in a ProjectLeader workbook:

- chemical samples can be displayed by their file name, or as line drawings that you can enlarge to view more clearly
- rows can be sorted
- grid lines can be hidden, or displayed as dotted, shaded gray, or solid black lines
- font size and type, and alignment of text can be changed, and text can be displayed as a molecular formula (i.e., numbers as subscripts)
- numbers can be displayed in scientific or standard notation (the default), with up to nine digits after a decimal point
- footnotes, column buttons, and row buttons can be displayed or hidden.

Changing the chemical sample display

By default, the ProjectLeader workbook displays chemical samples as line drawings. However, you can choose to display the names of the chemical samples instead.

Individual line drawings can be scaled in the workbook, so that you can view the molecular structure more clearly.

To display or hide a chemical sample

1. Select a chemical sample by clicking on it in the Chemical Sample column.

   The cell is highlighted in black to show that it is selected.

2. Choose **Format** | **Structure** to enable or disable the structure view.

   A check mark is displayed next to the menu option if it is enabled. When it is enabled, the chemical samples are displayed as line drawings. When it is disabled, the chemical samples are

displayed as names.

To scale a structure line drawing in a worksheet

1. Position the cursor at the bottom of the row button adjacent to the line drawing that you want to scale.

   The cursor changes into a crosshair shape.

2. Click and drag downwards to increase the depth of the row.

   The adjacent molecular line drawing increases in size in proportion to the row button.

3. Position the cursor to the right of the column button **A**.

   The cursor changes into a crosshair shape.

4. Click and drag to the right to increase the width of the column.

   All molecular line drawings in the Chemical Sample column increase in size in proportion to the column button **A**.

Sorting rows

You can sort the rows in a ProjectLeader worksheet according to the following properties:

- in ascending (A to Z, or numeric) or descending (Z to A, or reverse numeric) order
- cell type, where data are sorted in the following order: numerics, molecular formula, then textual data
- text only, where formulae for the molecula ordering convention is observed: carbon atoms, hydrogen atoms, then remaining atoms in alphabetical order
- text handling, where the case of textual data is observed.

To sort rows

1. Select the column by which you want to sort the rows.
2. Choose **View | Sort** to display the Sort dialog box.

   The column that you selected is displayed from the drop-down list in the **Primary Key** panel.

3. Select either **Ascending** (A to Z, or numeric) or **Descending** (Z to A, or reverse numeric) order from the **Primary Key** panel.
4. If required, select a column to be used as a secondary key in the **Secondary Key** panel from the drop-down list.
5. Select either **Ascending** or **Descending** from the **Secondary Key** panel.
6. Select the **Options** tab.

   This enables you to determine the sort mode, and text handling.
7. In the **Sort Mode** panel, do one of the following:
   - select **Cell type** to sort numerical data first
   - select **Text only** to sort only textual data.
8. If required, do one of the following in the **Text Handling** panel:
   - select **Case sensitive** to sort textual data so that capitals have a higher priority
   - select **Case insensitive** to sort textual data regardless of case.
9. Select **OK** to accept the changes, and to close the Sort dialog box.

   The data in the column is sorted according to your preferences.

📖 TIP Press the **right** mouse button, and select **Sort Ascending** to sort rows from A to Z, or in numeric order. Press the **right** mouse button, and select **Sort Descending** to sort rows from Z to A, or in reverse numeric order.

Changing the grid line display

To change the grid line display

Choose one of the following:

- **View | Grid Line | None**
- **View | Grid Line | Dotted**
- **View | Grid Line | Gray**
- **View | Grid Line | Solid**.

The grid lines in the worksheet change to the selected style.

Changing the text display

To display text in a different font size or type

1. Select the cells containing the text you want to change.
2. Choose **Format** | **Font** to display the Font dialog box.
3. Select the **Font**, **Font style**, and **Size** from the scrolling lists, or edit the text box directly.
4. Select **OK** to apply the changes, and to close the Font dialog box.

To change text alignment

1. Select the cells containing the text you want to change, then choose one of the following:
   - **Format** | **Left**
   - **Format** | **Center**
   - **Format** | **Right**.

   The alignment of the selected text changes.

To display text as a molecular formula

1. Select the cells containing the text you want to change.
2. Choose **Format** | **Molecular Formula**.

   The selected text is displayed with the numbers as subscripts.
3. Choose **Format** | **Normal Text** to revert the display to normal text.

Changing the numerical display

Select the cells containing the numbers you want to change, and choose one of the following from the Format menu:

Scientific Notation	to display numbers in scientific notation
Standard Notation	to display numbers in standard notation
Digits after Decimal	to set the number of decimal places to display

Hiding and displaying worksheet features

To hide or display column or row buttons

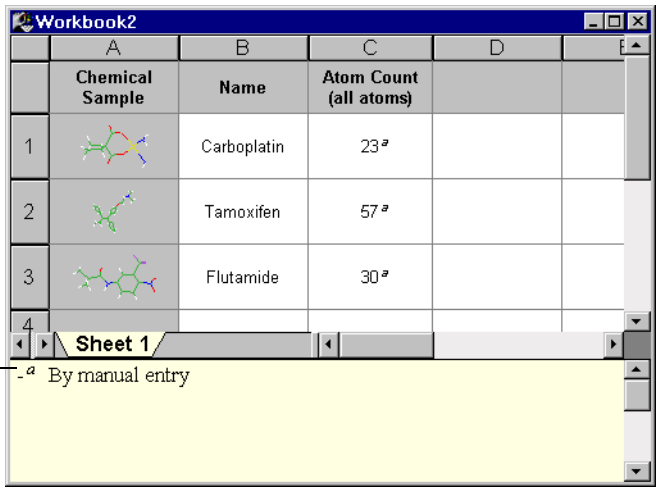
1. Choose:
   - **View** | **Column Labels** to display or hide column labels
   - **View** | **Row Labels** to display or hide row labels.

   The menu option has a check mark next to it when the labels are displayed, and no check mark when the labels are hidden.

Using worksheet footnotes

ProjectLeader lets you add footnotes to a cell, and choose whether to display them or not. If a worksheet has a footnote, a small icon is displayed in the worksheet cell.

When a cell is selected, any footnotes associated with it are displayed underneath the ProjectLeader worksheet in the footnote display area, as shown in the following diagram.



To add a footnote to a cell

1. Select the cell by clicking on it.
2. Choose **View** | **Cell Information** to display the Cell Information dialog box.

3. Click in the **Footnote** panel then enter the footnote that you want to add.
4. Select **OK** to close the Cell Information dialog box.

   The footnote is displayed in a scrolling window at the bottom of the worksheet.

To display or hide footnotes

1. Choose **View** | **Footnote** to display or hide footnotes.

   A check mark next to the menu option indicates whether footnotes are currently displayed. Footnotes are displayed in a scrolling section below the worksheet.

Viewing cell information

You can view the following information about a cell:

- the property it displays
- the procedure used to calculate the property
- the date and time the information was last updated.

To view or edit cell information

1. Select the cell by clicking on it.
2. Choose **View** | **Cell Information** to display the Cell Information dialog box.

   The **Cell text** text box displays the contents of the cell.

   A scrolling list displays the chemical sample property that the cell contains, the procedure used to calculate the property, and when the information was last updated.

   The **Footnote** section displays any footnotes attached to the cell.
3. Double-click in the **Cell text** text box to edit the cell contents.
4. Click in the **Footnote** section to add or edit a footnote for the cell.
5. Select **OK** to make the changes and to close the Cell Information dialog box.

Printing files

ProjectLeader enables you to print a copy of a worksheet view, or a scatter plot.

The following sections describe how to:

- preview a printout
- change print settings
- print a ProjectLeader worksheet or scatter plot.

Previewing a printout

ProjectLeader enables you to view the appearance of a printout before you print.

To preview a printout

1. Activate the document window whose contents you want to preview by clicking on the window.
2. Choose **File | Print Preview** to enter print preview mode.

   The contents of the window are displayed framed in a page as they would appear in a printout.
3. To exit print preview mode, choose **Close**.

   ProjectLeader returns you to the document window.

Choosing print options

You can change the following print options in ProjectLeader:

- which printer to use and its properties
- page orientation of a printout
- paper size and source.

To specify a printer and its properties

1. Choose **File | Page Setup** to display the Page Setup dialog box.

2. Select **Printer** to display a further Page Setup dialog box.
3. To use a different printer from the one displayed in the **Printer** panel, select the arrow button in the **Name** box and choose a printer from the drop-down list.

   The printer's status, type, and location are displayed in the **Printer** panel of the dialog box.
4. To change the properties of the printer, select **Properties** to display a dialog box containing specific options for your printer type.
5. Select the **Page Setup** or **Advanced** tab to display and select the options relevant to your printer.
6. Select **OK** to close the dialog box of document properties and to return to the Page Setup dialog box.
7. Select **OK** in the Page Setup dialog box to save the selected printer and its properties and to close the Page Setup dialog box.

To change page orientation of a printout

1. Choose **File** | **Page Setup** to display the Page Setup dialog box.
2. In the **Orientation** panel, select one of the following:
   - select the **Portrait** radio button to print portrait images, where the paper is longer than it is wider
   - select the **Landscape** radio button to print landscape images, where the paper is wider than it is longer.
3. Select **OK** to save the page orientation and to close the Page Setup dialog box.

To change paper size and source

1. Choose **File** | **Page Setup** to display the Page Setup dialog box.
2. Select the arrow button in the **Size** box, located in the **Paper** panel, and choose a paper size from the drop-down list.
3. Select the arrow button in the **Source** box, located in the **Paper** panel, and choose a paper source from the drop-down list.
4. Select **OK** to save the paper size and source settings, and to close the Page Setup dialog box.

Printing a ProjectLeader window

You can print a ProjectLeader worksheet or scatter plot.

To print a ProjectLeader window to a printer

1. Activate the document window whose contents you want to print by clicking on the window.
2. Do one of the following:
   - Choose **File** | **Print**
   - Press **Ctrl P**.

   The Print dialog box is displayed.
3. In the **Copies** panel of the Print dialog box, do one of the following:
   - In the **Number of Copies** text box, select the up arrow to increase the number of copies of the printout you require, or select the down arrow button to decrease the number of copies you require.
   - Click in the **Number of Copies** text box and enter the number of printouts you require.
4. Select **OK** to print the contents of the active document window to a printer and to close the Print dialog box.

Exporting a ProjectLeader worksheet

You can export a ProjectLeader worksheet in `.sdf` file format for use in other applications, such as chemical database programs.

To export a worksheet

1. Select the data that you want to export. If you want to export the entire worksheet, select the worksheet button in the top right-hand corner of the worksheet.
2. Choose **File** | **Export** to display the Save As dialog box.
3. Click in the **File name** text box and type a name for the new file.
4. Choose **Files (*.sdf)** from the **Save as type** drop-down list.
5. Select **Save** to save the `.sdf` file, and to close the Save As dialog box.

Saving a ProjectLeader project

ProjectLeader projects can be saved as project files. This enables you to save a project that you have been working on, then open it again and continue working on it from where you stopped.

One ProjectLeader workbook is saved in each project. If you have more than one workbook open when you save a workbook as a project, ProjectLeader will prompt you to supply a different name for each workbook so that each workbook is saved in a different project.|

To save a ProjectLeader project

1. Choose **File | Save**.

   If you have not already defined a name for the project, the Save As dialog box is opened.

2. Move to the directory in which you want to save the project.
3. Enter a name for the project in the **File name** text box.
4. Select **Save** to save the project.

   If you have more than one workbook that has not been saved as a project, the Save as dialog box remains open so that you can save the other projects.

5. Save all of the projects that you want to save. Select **Cancel** to skip any projects that you do not want to save.

Quitting ProjectLeader

To quit ProjectLeader

1. Choose **File** | **Exit**.

   If you have any unsaved changes in open windows, you are prompted to save changes.

2. Do one of the following:
   - Select **Save** to save the changes, before quitting ProjectLeader.
   - Select **Discard** to quit ProjectLeader without saving the changes.
   - Select **Cancel** to keep ProjectLeader running.

13 Optimization and Energy Calculations

Overview

This chapter describes:

- optimizing with CAChe to discover low energy conformations of your molecule
- calculating the current energy of a chemical sample.

Contents

Optimizing chemical samples **13-2**
Classical or quantum mechanics? 13-3
Optimizing with classical mechanics 13-3
Optimizing with quantum mechanics 13-4
Selective optimization **13-6**
Optimizing substituted portions of a molecule 13-6
Investigating reactive sites at the surface of enzymes 13-8
Maintaining mutual orientations 13-8
Viewing optimized structures **13-10**
Calculating current energy **13-11**
Calculating current energy with classical mechanics 13-11
Calculating current energy with quantum mechanics 13-11
Including solvation effects 13-12

Optimizing chemical samples

Optimization involves finding the most stable geometry, or minimum energy structure, of a chemical sample.

The lowest energy, or optimum structure, of a conformation of a molecule displays characteristics and properties that are more likely to reflect the true behavior of a chemical sample. Therefore, using optimization in CAChe enables you to achieve more accurate results when analyzing molecular characteristics.

Because of this, most CAChe experimental procedures begin with optimizing your chemical sample.

📖 NOTE You might not always want to optimize the sample; for example, if the sample is already in a low-energy geometry from a previous experiment.
In this situation, choose the existing geometry and wavefunction procedure for your experiment. This procedure uses existing geometry and wavefunction data from previous experiments on the chemical sample.

CAChe uses both classical molecular mechanics and semi-empirical quantum mechanics to find minimum energy conformations of your molecule. You can combine both methods of optimization in a CAChe experiment. For example, you can optimize a molecule using classical mechanics first, and then refine the structure using quantum mechanics.

CAChe optimization procedures also enable you to:

- include solvation effects of water while optimizing your molecule.



Refer to *"Modeling solvent effects with COSMO"*, p 20-19, for more information on experimental procedures that include solvation effects.

Classical or quantum mechanics?

Classical mechanical methods are much faster than using quantum mechanical calculations. Also, experiments tend to yield similar or more accurate optimized geometries when applying classical mechanics to discover a low-energy structure.

However, if your sample is in a state where electronic effects have a significant impact on the structure (e.g., a transition state), its geometry cannot be refined by a classical approach. Similarly, classical mechanical experiments do not yield any molecular orbital information.

Many CAChe procedures perform an optimization using classical mechanics first, before refining the resulting structure using one of the quantum mechanics techniques. This often reduces computation time, while providing molecular orbital information.

Optimizing with classical mechanics

CAChe examines bond angles and atom distances in your molecule and compares its geometry to the classical mechanical ideal value. Deviations from the ideal accumulate a relative energy quantity known as steric or potential energy.

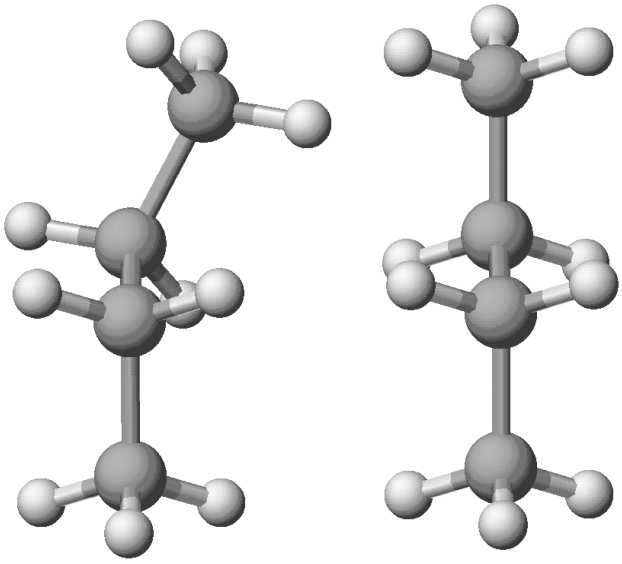
CAChe calculates these deviations from the ideal, and optimizes a molecule by moving its atoms to lower the sum of the deviations (and thus lower the steric energy) until energy changes are negligible.

For example, the deviation of a dihedral angle from a staggered conformation adds to the steric energy of butane. Other factors, such as hydrogen bonding, are stabilizing and reduce the total steric energy for your sample.

CAChe performs as many optimization iterations as necessary, and stops when the steric energy change between iterations becomes acceptably small. At the end of an optimization, your chemical sample's geometry corresponds to a steric energy minimum, although it might not be the absolute global minimum.

The following example shows how CAChe optimizes a butane molecule with a strained dihedral angle, so that the atoms of the

optimized molecule do not deviate from the classical mechanical ideal, and therefore steric energy is minimized.



A strained dihedral angle in butane

A perfectly staggered dihedral angle

Optimizing with quantum mechanics

Quantum mechanics uses the presence and positions of electrons between atoms to calculate a minimum energy structure, based on the Schrödinger equation.

Quantum mechanical procedures in CAChe calculate an energy related to the heat of formation for different structures of the molecule, until the energy is minimized.

Quantum mechanics also allows you to compare heat of formation values for different chemical samples, as well as comparing the energy values of different conformations of the same molecule.

Heat of formation energy values produced from quantum mechanical computations can be:

- directly compared
- adjusted, then compared to experimental heats of formation.

📖 NOTE Optimization with quantum mechanics is not available with Personal CAChe.

Selective optimization

You can optimize only selected portions of your molecule, rather than the whole structure.

To do this, you lock atom coordinates and specified geometry labels so that atoms remain in the same position, and atom distances and bond angles remain at a constant value, during an experiment.

All computational applications, apart from ZINDO, recognize locked atom coordinates and locked geometry labels.



Refer to *"Locking geometry labels"*, p 8-29, and *"Locking atoms"*, p 8-32, for information on applying locks.

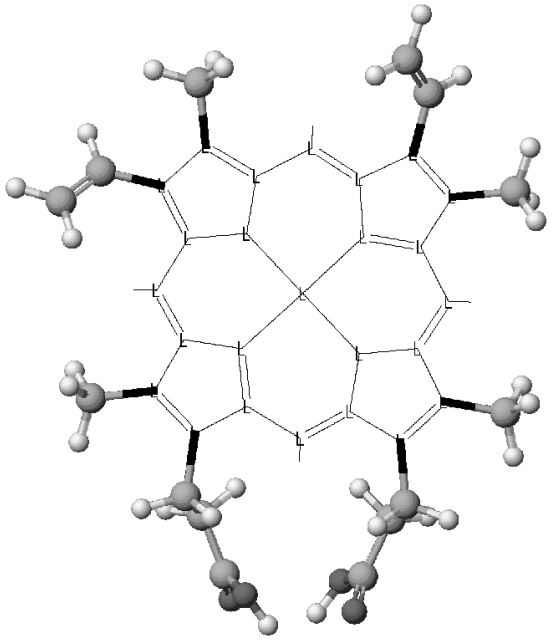
There is no set procedure for selective optimization, but the following sections describe situations where optimization of only one portion only of a chemical sample can be used.

Optimizing substituted portions of a molecule

If you know the geometry of the structure for a sample closely related to your molecule, you may want to explore the most likely geometry of sites where you made substitutions.

You can optimize the substituted portion of the sample, while leaving the section for which data exists untouched, whereas normal optimizing would cause structural adjustments throughout the whole chemical sample.

The following example shows a molecular structure where the core atoms of a molecule could be locked while allowing the pendant groups to optimize.



Follow the steps below to perform a selective optimization.

To optimize selected portions only of a molecule

1. Select all the atoms you want to remain unchanged by clicking on the first one with the Select tool, holding down the **Shift** key, and clicking on the rest of the atoms you do not want to optimize.
2. Choose **Adjust** | **Lock**.

   An **L** is displayed in the workspace to indicate that the atoms are locked.
3. Use the Atom/Bond tool to draw the atoms and bonds that comprise the substituted portion of the molecule by clicking and dragging in the workspace.

   This is the portion that you want to optimize.
4. Choose **File** | **Save** to save the chemical sample file.
5. Run the optimization experiment of your choice.

   The locked atoms remain fixed at their workspace coordinates, while the rest of the chemical sample is optimized.

Investigating reactive sites at the surface of enzymes

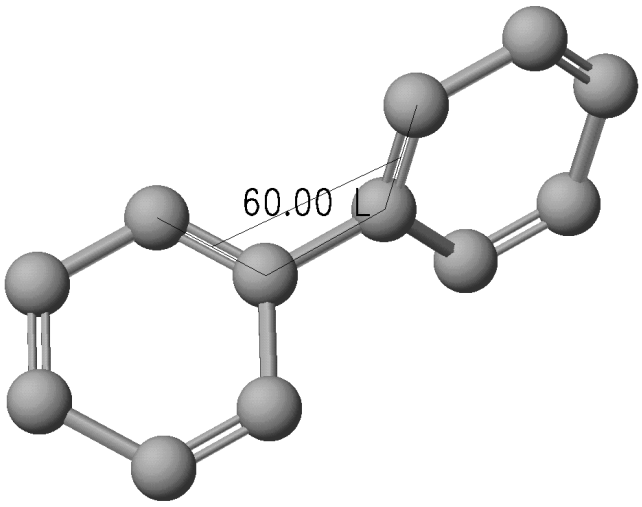
Selectively locking geometry attributes can also be helpful when you are investigating reactive sites at the surface of enzymes. The only difference between this example and the previous one is that the chemical sample file you optimize contains two different structures: the substrate, which is completely free to optimize, and the enzyme, whose reactive site is also free to optimize but whose remaining structural mass can be locked.

Performing the optimization this way saves a great deal of time since the bulk of the chemical sample is not being adjusted.

Maintaining mutual orientations

If your chemical sample has a biphenyl structure, you may want to investigate the molecule while the two rings are kept at a 60° dihedral angle.

The following example shows a molecular structure where you may want to lock the angle between two rings before performing an optimization.



Follow the steps below to perform a selective optimization where the rings are kept at a constant orientation.

To optimize a molecule while retaining a fixed dihedral angle

1. Select all the participating atoms of the dihedral angle by clicking on the first one with the Select tool, holding down the **Shift** key, and clicking on the second, third, and fourth atoms of the dihedral angle. Ensure that the first atom you select is the atom that you want to move if you are adjusting the dihedral angle.
2. Choose **Adjust** | **Dihedral angle** to display the Set Dihedral Angle dialog box.
3. Click in the **Angle** text box and type `60.00`.
4. Select the **Define Geometry Label** check box.
5. Select the **Lock Geometry** radio button.
6. Select **OK** to close the Set Dihedral Angle dialog box.

   A geometry label identifies the participating atoms and displays the value of the dihedral angle and an **L** in the workspace to indicate that the angle is locked.
7. Choose **File** | **Save** to save the chemical sample file.
8. Run the optimization experiment of your choice.

Viewing optimized structures

When you optimize a chemical sample, CAChe automatically saves the optimized structure in the chemical sample file.

Sometimes, viewing the optimized structure alone can answer questions about factors that affect a molecule's geometry, such as steric interactions.

However, you often need to view the differences between the original and the optimized structure. If you save the chemical sample file using a different file name before optimizing, the original structure and the optimized one are both available to compare.

One way to view differences is to superimpose one structure on the other. You can also compare distances and angles using geometry labels to measure the geometry of both structures precisely.



Refer to Chapter 8, *"Investigating Molecular Geometry"*, for details about superimposing molecules.

Calculating current energy

You can measure the energy of a chemical sample in its existing geometry, without changing or optimizing its current geometry.

CAChe provides procedures that use one of the following:

- classical mechanics, which calculates the current steric or potential energy of the molecule
- quantum mechanics, which calculates the heat of formation of the molecule.

CAChe current energy procedures also enable you to:

- include solvation effects of water while calculating the current energy of your molecule.

Calculating current energy with classical mechanics

CAChe examines bond angles and atom distances in your molecule and compares the geometry to the classical mechanical ideal value. Deviations from the ideal accumulate a relative energy quantity known as steric or potential energy.

CAChe calculates these deviations from the ideal and computes a steric or potential energy value for the molecule without altering its structure.

Calculating current energy with quantum mechanics

Quantum mechanics uses the presence and positions of electrons between atoms to calculate the energy of a structure based on the Schrödinger equation. Quantum mechanical procedures in CAChe calculate an energy related to the heat of formation for a molecule.

📖 NOTE Calculating current energy using quantum mechanics is not available in Personal CAChe.

Including solvation effects

CAChe allows you to include water solvent effects in a current energy experiment by using COSMO.



Refer to *"Modeling solvent effects with COSMO"*, p 20-19, for more information on experimental procedures that include solvation effects.

14 Investigating Low-energy Conformations

Overview

This chapter describes how to investigate a series of low-energy conformations of your molecule by generating and analyzing the following energy maps:

- a rigid energy map
- an optimized energy map
- a sequence of conformations
- a dynamics trajectory.

Contents

Generating energy maps	**14-2**	**Viewing map files**	**14-12**
Preparing your chemical sample file	14-5	Map file windows	14-12
Generating a rigid energy map	14-6	Map file display options	14-15
Generating an optimized energy map	14-7	Analyzing map files	14-22
Generating a sequence of conformations	14-9	Animating map files	14-26
Generating a dynamics trajectory	14-10	Saving map files	14-30

Generating energy maps

When you optimize a sample, the resulting low-energy geometry is based on the original geometry that you started with.

By varying the geometry of your sample into numerous different conformations and measuring the energy of each, CAChe can investigate the existence of other low-energy conformations for your molecule based on a different geometry.

CAChe generates energy map files (`*.map`) from the following experiments:

- rigid energy map (`energy.map`)
- optimized energy map (`energy.map`)
- sequence of conformations (`seqsrch.map`)
- dynamics trajectory (`dynamics.map`)
- reaction path (`irc1.map`, `irc-1.map`, `drc1.map`, `drc-1.map`).



Refer to Chapter 17, *"Investigating Reactions"*, for details about reaction paths.

Map files are also called assemblage files because they are an assemblage of structure/energy pairs. Map files enable you to visualize the relationships between sample conformations and their energy, plotted in a two- or three-dimensional graph.

Energy maps are generated by varying specified coordinates of your molecule to create a series of conformations. The energy of each conformation is plotted in a two- or three-dimensional graph so that you can easily locate low energy conformations separated by high-energy barriers. This makes it possible to locate a global rather than a local energy minimum for the molecule.

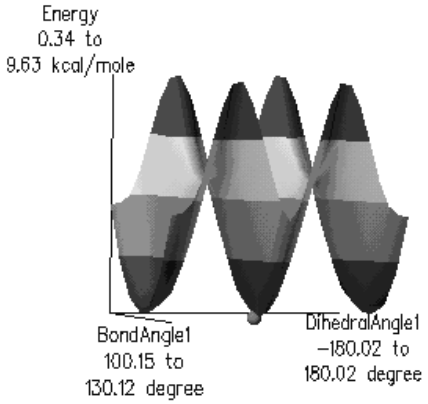
CAChe allows you to:

- view and manipulate each conformation of your molecule beside the energy graph

- view the corresponding conformation for any point on the graph, and vice versa
- animate the conformations so that you can view each structure generated, while the energy map displays the graph location of each conformation.

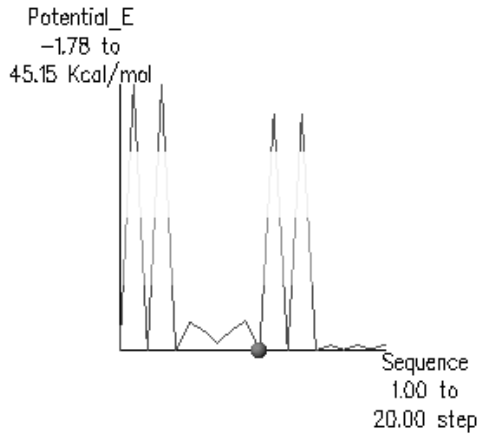
CAChe generates the following types of energy maps:

- rigid or optimized energy maps (`energy.map`), where the potential energy of each conformation is measured, and each conformation is either not optimized (rigid map) or optimized (optimized map). An optimized energy map (`energy.map`) is also generated when you run a map reaction experiment.



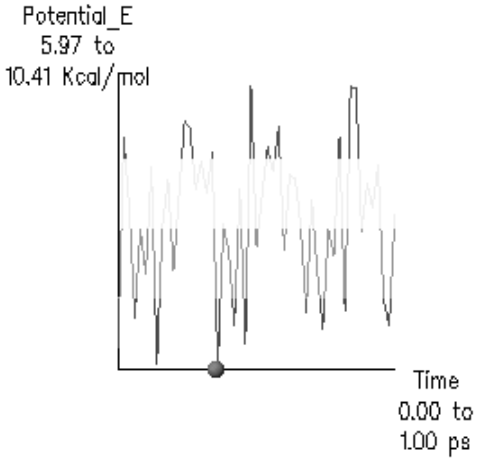
Three-dimensional rigid energy graph

- a sequence of conformations (`seqsrch.map`), where low-energy conformations only are generated by finding a low-energy value for a coordinate in the molecule, and holding that coordinate at the low energy value while repeating the process for each specified coordinate in the molecule



Sequence of conformations graph

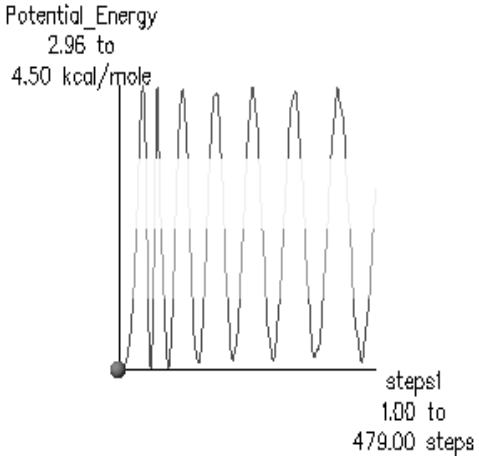
- a dynamics trajectory (`dynamics.map`), where kinetic energy is added to a molecule by randomly assigning velocities to atoms. As the calculation proceeds, kinetic energy is transformed into potential energy. The potential energy of resulting conformations is plotted against time.



Dynamics trajectory graph

- a reaction path (`irc.map`, `irc-1.map`, `drc1.map`, `drc-1.map`), where two internal coordinates of a chemical sample are varied to form the principal deformations occurring in the

course of a reaction. A series of reaction path structures are calculated between the transition state structure (deformed structure) to either the product or reactant molecule.



Reaction path graph

Refer to Chapter 17, *"Investigating Reactions"*, for more information on map reaction experiments.

Preparing your chemical sample file

Before generating a rigid or optimized energy map, or sequence of conformations, you must first add search labels to the atom distances and bond angles that you want varied in your molecule to generate the series of conformations. You do not have to add search labels to perform a dynamics trajectory or reaction path experiment.

CAChe steps the search labels (a form of geometry label) through the range of values that you specified when defining the search labels, to form the conformations and measure the energy of each structure. You can define search labels for atom distances, bond angles, improper torsion angles, and dihedral angles.

Refer to Chapter 8, *"Investigating Molecular Geometry"*, for more information on adding search labels to a chemical sample.

Generating a rigid energy map

CAChe steps the search labels through their defined range of values and computes the energies of each resulting conformation. For example, if you define two search labels, each with 10 steps, your energy map will contain 121 conformations (11^2), because 10 steps results in 11 conformations, and each one is tested in combination with all other possibilities.

CAChe provides procedures that use one of the following:

- classical mechanics, which generates a potential energy rigid map
- quantum mechanics, which generates a heat of formation rigid map.

📖 NOTE You cannot generate a rigid energy map using quantum mechanics with Personal CAChe or BioCAChe.

A rigid energy map calculation keeps the structure rigid at the defined search label values. The unoptimized conformational energy is plotted as a function of the position of any two of the structural elements to create the rigid map.

An optimized map optimizes each conformation resulting from the search label values. Both rigid and optimized maps are useful for investigating how energy changes as a function of specific geometry attributes in your molecule.

Refer to *"Generating an optimized energy map"*, p 14-7, for more information.

Generating a rigid energy map with classical mechanics

Classical mechanical procedures measure the potential energy of each conformation of a molecule formed by varying the search labels. The labeled bond angles and atom distances in your molecule are examined and compared to the classical mechanical ideal geometry. Deviations from the ideal accumulate potential energy, which is measured and plotted in an energy graph for each conformation.

You can add up to eight search labels to generate a rigid energy map using classical mechanical procedures. However, because of the time required to complete the calculations, it is more practical to add a maximum of three or four search labels to one molecule.

Generating a rigid energy map with quantum mechanics

Quantum mechanical procedures measure the heat of formation of each conformation of a molecule formed by varying the search labels. The presence and position of electrons between atoms is measured in every conformation formed by the search labels, and heat of formation is calculated, based on the Schrödinger equation.

You are limited to a maximum of two search labels in your molecule.

If you use one search label the result is a reaction coordinate search. If you use two search labels, the result is a grid search.

Energy maps generated using quantum mechanics are useful for mapping bond breaking and bond formation in a molecule.

📖 NOTE You cannot generate a rigid energy map using quantum mechanics with Personal CAChe or BioCAChe.

Generating an optimized energy map

An optimized energy map is similar to a rigid map, except that each conformation formed by the varying search labels is optimized before the energy is calculated.

CAChe steps the search labels through their defined range of values and optimizes each resulting conformation. An optimized map takes much longer to generate than a rigid map, because of the optimization step.

CAChe provides procedures that use one of the following:

- classical mechanics, which generates a potential energy optimized map
- quantum mechanics, which generates a heat of formation optimized map.

> 🕮 NOTE You cannot generate an optimized energy map using quantum mechanics with Personal CAChe or BioCAChe.

The optimized conformational energy is plotted as a function of the lowest-energy position of any two of the structural elements to create the optimized map.

Generating an optimized energy map with classical mechanics

Classical mechanical procedures measure the potential energy of each conformation of a molecule formed by varying the search labels. Each conformation is then optimized by lowering deviations from classical mechanical ideal geometry. The potential energy of each optimized conformation is then plotted in an energy graph.

You can add up to eight search labels to generate an optimized energy map using classical mechanical procedures. However, because of the time required to complete the calculations, it is more practical to add a maximum of three or four search labels to one molecule.

Generating an optimized energy map with quantum mechanics

Quantum mechanical procedures measure the heat of formation of each conformation of a molecule formed by varying the search labels. Each conformation is then optimized by measuring the presence and positions of electrons based on the Schrödinger equation. The heat of formation of each optimized conformation is then plotted in an energy graph.

You are limited to a maximum of two search labels in your molecule.

If you use one search label, the result is a reaction coordinate search. If you use two search labels, the result is a grid search.

Energy maps generated using quantum mechanics are useful for mapping bond breaking and bond formation in a molecule.

> 🕮 NOTE You cannot generate an optimized energy map using quantum mechanics in Personal CAChe or BioCAChe.

Investigating water solvent effects

You can include water solvent effects in rigid or optimized energy map experiments, and map reaction experiments.

Refer to *"Modeling solvent effects with COSMO"*, p 20-19, for more information on experimental procedures that include solvation effects.

Generating a sequence of conformations

A sequence of conformations, or sequential search, is similar to an optimized map, but offers a faster method to arrive at purely low-energy conformations, rather than the combination of low- and high-energy structures that an optimized map produces.

Instead of evaluating and optimizing the energy of all possible combinations of search label values, the sequence of conformations finds the lowest energy value of each search label in turn, and locks each label at its lowest value, before proceeding to the next one. In this way, only low-energy conformations are generated.

The following procedures are available for a sequence of conformations experiment:

- one pass search, which evaluates only one low energy value for each search label
- multiple pass search, which evaluates up to three low energy values for each search label.

Sequential searches are often an efficient way to get closer to the global minimum energy value for a molecule. The resulting map file contains local energy minima without high-energy barriers between them.

Sequential searches always generate a two-dimensional graph, regardless of the number of search labels in the chemical sample file. The horizontal axis is simply the sequence in which the conformations were evaluated, and the vertical axis displays the potential energy for the particular conformation.

Sequential searches can only be performed by Mechanics using classical mechanical methods. You can use an unlimited number of search labels in a sequence of conformations experiment.

TIP To use a large number of search labels in a sequence of conformations experiment, you can add dihedral angle search labels automatically using the Geometry Label Wizard.

Refer to *"Defining search labels automatically"*, p 8-41, for details about using the Geometry Label Wizard.

Generating a dynamics trajectory

Dynamics trajectory experiments allow you to visualize the movement of atoms that results from adding thermal energy to the molecule.

Initially, the energy is added in the form of kinetic energy by randomly assigning velocities to atoms. As the calculation proceeds, however, some kinetic energy is transformed into potential energy. The total energy in the system is conserved throughout the experiment.

You do not need to add search labels to a sample before performing a dynamics trajectory experiment, so your chemical sample file requires no preparation.

Therefore, a dynamics trajectory experiment is a faster alternative to a rigid map, optimized map, or sequence of conformations experiment, which can take too much time to prepare and generate for large molecules.

The resulting energy map from a dynamics trajectory allows you to view conformations beside a two-dimensional energy graph, which can be used to:

- identify low-energy conformations
- gain useful information regarding the relative rigidity of a structure.

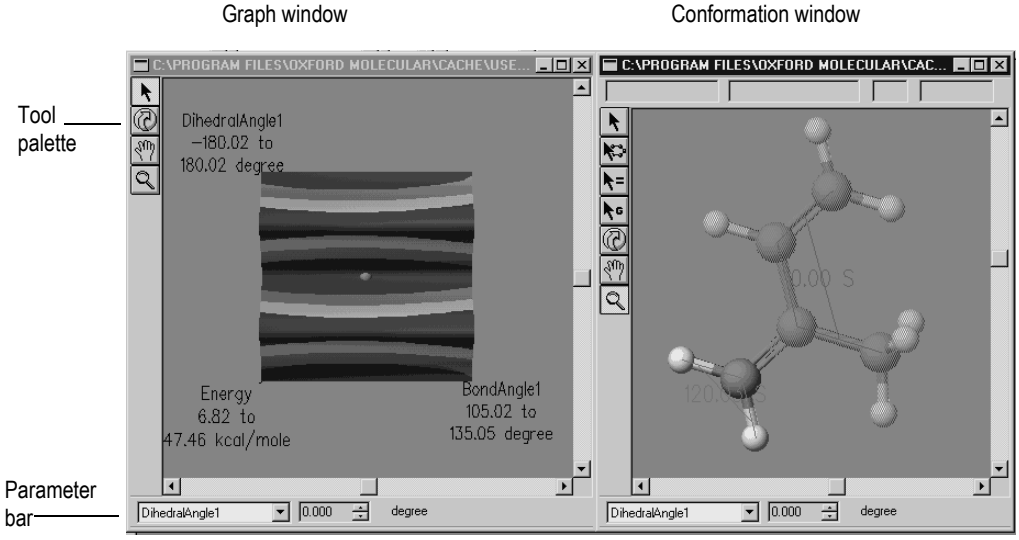
The horizontal axis corresponds to the time frame in which the structures are sampled, and the vertical axis represents the energy of the resulting conformation.

Low-energy structures in a trajectory map are not truly energy minima. These structures are good starting points for a geometry optimization, which leads to a more accurate minimum energy geometry.

📖 NOTE You cannot generate a dynamics trajectory in Personal CAChe.

Viewing map files

When you open a map file, two windows open side by side, as shown in the following example.



To open a map file

1. Choose **File** | **Open** to display the Open dialog box.
2. Double-click on the `Cache` folder to open it.
3. Click and drag on the scroll bar of the scrolling list to locate the `.map` folder belonging to the relevant chemical sample file and double-click on the `.map` folder to open it.
4. Select the arrow button in the **Files of type** box and choose **Map (*.map)** from the drop-down list.
5. Double-click on the required map file to open it.

Map file windows

The structure displayed in the right window (the conformation window) is the lowest energy conformation of all the structures generated by the experiment. Its energy value is displayed in the parameter bar at the bottom of the window, and a small spherical

marker indicates the corresponding energy location in the graph in the left window (the graph window).

The graph displayed in the graph window can be rotated in two or three dimensions. The colors of the graph in the graph window represent the relative energies of graph locations and their equivalent conformations.

The two windows are interactive. If you click on a graph location in the graph window, the conformation window displays the conformation that corresponds to the selected point on the graph. You can also move the marker step by step along the graph using the up, down, left, and right arrow keys.

The conformation window displays the corresponding structure as the marker moves throughout the graph.

Both windows contain:

- a tool palette, similar to the workspace tool palette
- a parameter bar that displays the x, y, and z parameters of the graph.

If you close a graph window and save the map file, the next time the file is opened, only the conformation window is displayed.

To display a graph window

1. Choose **Window | New Graph Window**.

   The graph window corresponding to the conformation window is displayed.

Using the tool palettes

The tool palette in both map file windows contain tools that function in exactly the same way as the workspace tools.



You can rotate, translate, and zoom in to the map and conformation window using the tools, and also select items with the three selection tools in the conformation window. Using the Select tool in the graph window changes the position of the spherical marker in the graph.

Refer to Chapter 5, *"Modifying Chemical Samples"*, for information on using the selection tools.

Refer to Chapter 7, *"Manipulating Molecules"*, for information on using the Rotate, Translate, and Scale tools.

Using the parameter bar

The parameter at the bottom of both windows contains a drop-down list from which you can choose to view in ascending or descending order:

- the values plotted along the x and y axes for a two-dimensional graph
- the values plotted along the x, y, and z axes for a three-dimensional graph.

To use the parameter bar

1. Select the arrow button in the left-hand parameter bar box to display a drop-down list of the parameters plotted along the graph axes. An example of left-hand and right-hand parameter bar boxes is shown below.



2. Choose the parameter whose values you want to view from the drop-down list.

   The right-hand parameter bar box displays the value for the currently selected graph position.

3. To increase or decrease the value of the selected parameter, select the up or down arrow buttons in the right-hand parameter bar box.

   The value jumps incrementally to the next value in the range.

4. The conformation window displays the conformation with the corresponding increased or decreased value, and the spherical marker moves to the graph location of the increased or decreased value.

   As you step through the range of values using the parameter bar, the marker in the graph window moves to the graph position that corresponds with the current value, and the conformation window displays the structure corresponding to the current parameter value.

Map file display options

CAChe enables you to change the display of components of the two map file windows, including:

- each window's parameter bar
- variables plotted along each graph axis
- graph color options
- axis attributes
- graph attributes.

Hiding the parameter bar

You can choose to hide the parameter bar on either a conformation or a graph window.

To hide the parameter bar

1. Activate the window whose parameter bar you want to hide.
2. Choose **Options | Show Parameter Bar.**

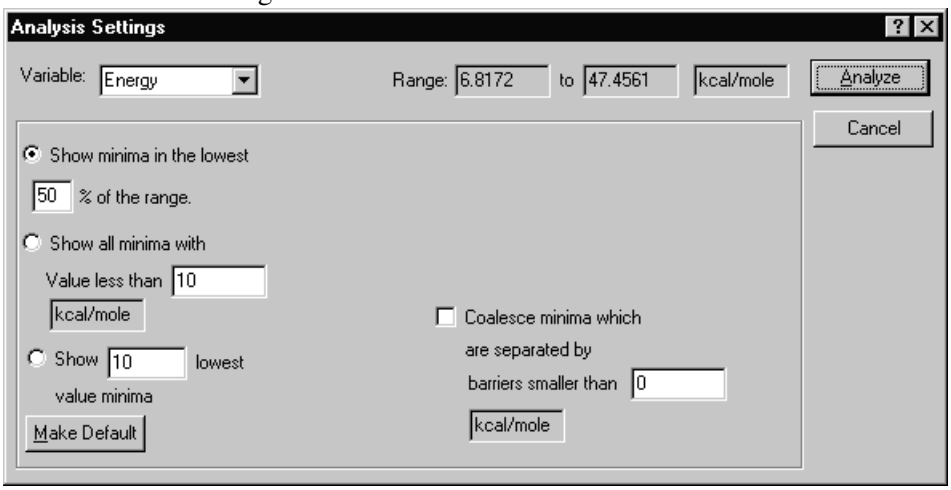
   The check mark next to the drop-down list option disappears to show that this option is disabled. The parameter bar in the active window is no longer displayed.

Changing the variables plotted along an axis

In a two-dimensional graph, energy is plotted on the y axis. In a three-dimensional graph, energy is plotted on the z axis. You can change the variables plotted along any axis. This is useful for displaying combinations of search label values if you generated a map with more than two search labels.

To change the variable plotted along any axis

1. Activate the graph window of the map file by clicking on it.
2. Choose **View | Graph Attributes** to display the Graph Attributes dialog box.



3. Select the arrow button in the **X**, **Y**, or **Z** boxes to display a drop-down list of variables which you can plot along that axis.
4. Choose the variable that you want to plot along the relevant axis from the **X**, **Y**, or **Z** drop-down lists.

   The drop-down lists include any search labels that are not currently assigned to a graph axis. These search labels are also listed at the left side of the Graph Attributes dialog box. The value shown for search labels not currently displayed in the graph is the value at which those labels are held constant.
5. Change the constant value for search labels not assigned an axis by selecting the up or down arrow button in the box displaying that label's current value.

   The value jumps incrementally based on the step size you defined for the search label.
6. Select **OK** to apply the changes to the graph and close the Graph Attributes dialog box.

Changing graph color

You can choose to color the graph function by:

- relative energy, where colors of the graph in the graph window represent the relative energies of graph locations and their equivalent conformations.
- constant color, where the graph function is displayed in one color only.

In trajectory files produced by Dynamics experiments, you can also choose to color a graph by:

- total energy
- kinetic energy
- potential energy
- temperature.

To change graph color

1. Activate the graph window of the map file by clicking on it.
2. Choose **View | Graph Attributes** to display the Graph Attributes dialog box.
3. Select the arrow button in the **Color By** box to display a drop-down list of color options.
4. Choose a color option from the drop-down list.
5. Select **OK** to apply color options to the map file graph and to close the Graph Attributes dialog box.

Changing axis attributes

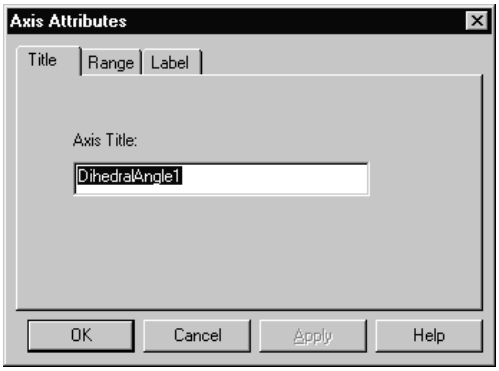
You can change the following axis attributes for individual axes:

- edit the range of values along a graph axis
- change the axis title
- hide or display axes, axis labels, and the range of values for an axis.

To change axis attributes

1. Activate the graph window of the map file by clicking on it.
2. Choose **View | Graph Attributes** to display the Graph Attributes dialog box.
3. Select **Attributes** under the box of the axis whose display options you want to change. For example, if you want to change display options for the X axis, choose **Attributes** under the **X** box.

   The Axis Attributes dialog box is displayed.



4. To change an axis title, select the **Title** tab to display the **Axis Title** text box.
5. Click in the **Axis Title** text box and type a title for the axis.
6. To change the range of values displayed on the axis, select the **Range** tab to display the **Maximum** and **Minimum** text boxes.
7. Click in the **Minimum** text box and type a minimum value for axis range.
8. Click in the **Maximum** text box and type a maximum value for the axis range.
9. To change axis labeling, select the **Label** tab to display a list of check boxes.
10. Select the **Show Axis** check box to hide the graph axis.

    The check mark is no longer displayed in the check box.
11. Select the **Show Axis Title** check box to hide the graph axis title.

    The check mark is no longer displayed in the check box.
12. Select the **Show Axis Range** check box to hide the graph axis range of values.

    The check mark is no longer displayed in the check box.
13. Select **OK** to save the axis display options and to close the Axis Attributes dialog box.
14. Select **OK** to close the Graph Attributes dialog box.

Changing graph attributes

You can also choose to hide or display the following graph attributes:

- all graph axes
- all axis labels
- the graph function
- the spherical graph marker.

To hide the graph axes of a graph window

1. Activate the graph window of the map file by clicking on it.
2. When the graph axes are visible, choose **View | Show Axes**.

   The check mark next to the drop-down list option disappears to show that the option is disabled. The axes of the graph are no longer displayed in the graph window.

To display the graph axes

1. Activate the graph window of the map file by clicking on it.
2. When the graph axes are hidden, choose **View | Show Axes**.

   A check mark is displayed next to the drop-down list option to show that it is enabled. The axes of the graph are displayed in the graph window.

To hide axis labels

1. Activate the graph window of the map file by clicking on it.
2. When axis labels are visible, choose **View | Show Axes Text**.

   A check mark is no longer displayed next to the drop-down list option to show that it is disabled. The axis labels of the graph are no longer displayed in the graph window.

To display axis labels

1. Activate the graph window of the map file by clicking on it.

2. When axis labels are hidden, choose **View | Show Axes Text**.

   A check mark is displayed next to the drop-down list option to show that it is enabled. The axis labels of the graph are displayed in the graph window.

To hide the graph function

1. Activate the graph window of the map file by clicking on it.
2. When the graph function is visible, choose **View | Show Graph Function**.

   A check mark is no longer displayed next to the drop-down list option to show that it is disabled. The graph function is no longer displayed in the graph window.

To display the graph function

1. Activate the graph window of the map file by clicking on it.
2. When the graph function is hidden, choose **View | Show Graph Function**.

   A check mark is displayed next to the drop-down list option to show that it is enabled. The graph function is displayed in the graph window.

To hide the graph marker

1. Activate the graph window of the map file by clicking on it.
2. When the graph marker is visible, choose **View | Show Marker**.

   A check mark is no longer displayed next to the drop-down list option to show that it is disabled. The spherical graph marker is no longer displayed in the graph window.

To display the graph marker

1. Activate the graph window of the map file by clicking on it.
2. When the graph marker is hidden, choose **View | Show Marker**.

   A check mark is displayed next to the drop-down list option to show that it is enabled. The spherical graph marker is displayed in the graph window.

Analyzing map files

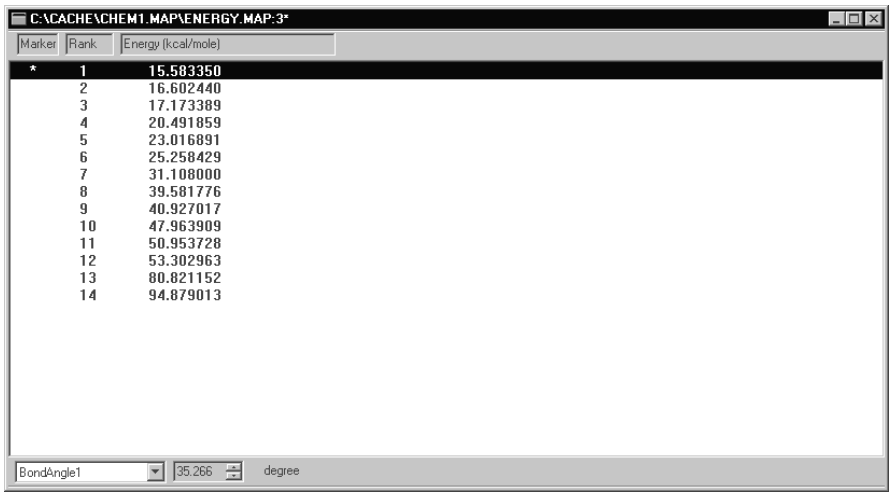
CAChe uses a conformational analysis window to list all of the conformations in your map file in ascending order of energy values. You can view the energy value of a conformation, plus the value of any other variable for that conformation.

To open a conformational analysis window

1. Activate a graph window or conformation window by clicking on it.
2. Choose **Window | New Conformational Analysis Window**.

   A conformational analysis window is displayed.

   The window lists the energies of the map file's conformations in order of ascending energy. The first energy value listed corresponds to the lowest energy minimum in the analysis. The conformational analysis window is interactive with the graph and conformation window.



3. Select a conformation in the conformational analysis window by clicking on the conformation in the list.

   An asterisk appears next to the selected conformation in the list. The conformation in the conformation window displays the conformation you selected in the list. The spherical marker in the graph window moves to the corresponding energy value in the

graph.

You may need to move the conformational analysis window to one side by clicking and dragging on its title bar to view the graph window and conformation window of the map file.

4. The parameter bar at the bottom of the conformational analysis window displays a parameter value for the selected conformation.
5. Select the arrow button in the right-hand box of the parameter bar to choose another parameter from a drop-down list.
6. Select the up or down arrow button in the left-hand box of the parameter bar to increase or decrease the value of the selected parameter in increments.

   The conformation window displays the conformation with the selected increased or decreased parameter value. The spherical marker in the graph window moves to the corresponding energy value in the graph.

   The resulting conformation no longer corresponds with the conformation you selected in the conformational analysis window. The asterisk next to the selected conformation in the list disappears, indicating that the graph location and conformation displayed by the map file windows is not one of the conformations listed in the conformational analysis window.
7. Do one of the following to view a conformation from a different perspective:

   Double-click on a conformation listed in the conformational analysis window to display a larger conformation window. Use this second conformation window to view the same conformation as appears in the first smaller conformation window from a different angle or from a different perspective.

   Choose **Window | New Conformation Window** or **Window | New Graph Window** to display as many map file windows as you want.
8. When you have finished viewing the list of conformations, select the Windows close button at the upper right corner of the conformational analysis window to close the window.
9. When you have finished viewing the graph or a conformation

from a different perspective, select the Windows close button at the upper right corner of extra copies of the graph or conformation window to close the window.

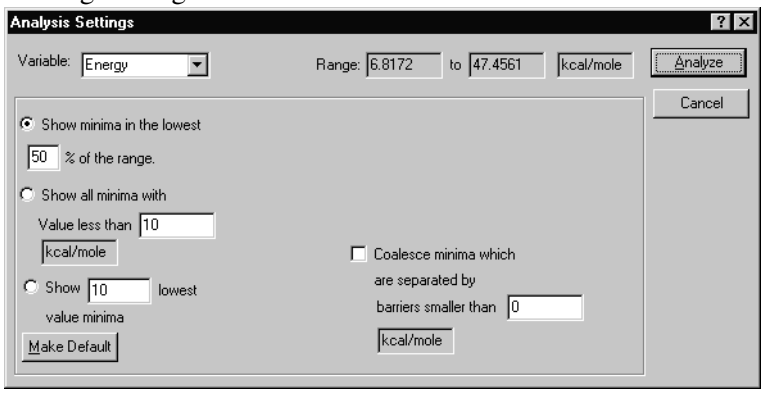
Specifying analysis criteria

You can change analysis settings to view selected portions only of the energy and conformational data in a map file. Control display of variable values in the following ways:

- display a percentage only of a range of values
- display only those conformations with a specified energy value
- display a specified number only of the lowest energy conformations
- eliminate low-energy conformations if they belong to shallow energy wells that are separated from adjacent lower minima by low energy barriers.

To specify analysis criteria

1. Activate a conformational analysis window by clicking on it.
2. Choose **Options | Analysis Settings** to display the Analysis Settings dialog box.



3. Select the arrow button in the **Variable** box to display a drop-down list of variables for which you can change settings.

4. To display a certain percentage only of low-energy conformations in the conformational analysis window, conformation window, and graph window, do the following:

   Select the **Show minima in the lowest** radio button so that it is enabled.

   Click in the **%** text box and type the percentage value for the range of low-energy conformations that you want to view.

5. To display only those low-energy conformations with a specified energy value, do the following:

   Select the **Show all minima with value less than** radio button so that it is enabled.

   Click in the **kcal/mole** text box and type the energy value for the range of low-energy conformations that you want to view.

6. To display a selected number only of low-energy conformations, do the following:

   - Select the **Show** radio button so that it is enabled.
   - Click in the **lowest value minima** text box and type the number of conformations with the lowest energy value that you want to view.

7. To eliminate minima occurring in shallow energy wells separated from adjacent lower minima by low energy barriers, do the following:

   - Select the **Coalesce minima which are separated by barriers smaller than** radio button so that it is enabled.
   - Click in the adjacent text box and type a value for the energy barrier.

   Energy wells separated by barriers smaller than the specified value result in the higher energy minimum being ignored.

8. Select **Analyze** to apply the specified analysis criteria to the map file windows, and to close the Analysis Settings dialog box.

Animating map files

Animating a map file runs through each conformation in the map file, while indicating the corresponding location on the energy graph for each location. You can visualize the following properties in each type of map file:

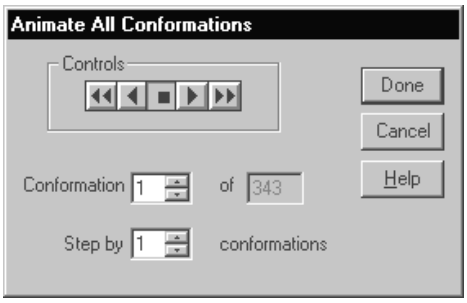
- animating a rigid or optimized map shows how the conformation defined by each step in a search label affects energy
- animating a sequence file shows a series of optimized structures
- animating a reaction path starts at the transition state conformation and proceeds toward either the reactant or the product
- animating a dynamics trajectory file shows you how long a sample remains in the same approximate conformation. If a conformation has a long life span, high energy barriers may exist that prevent the structure from changing. Such a conformation might be a good starting structure for further analysis.

To animate a map file

1. Activate a graph window, conformation window, or conformational analysis window by clicking on the window.
2. Choose one of the following:
   - **Edit | Animate Along Axis** (if you activated a graph window) to display the Animate Along Horizontal Axis dialog box.
   - **Edit | Animate All Conformations** (if you activated a conformation window) to display the Animate All Conformations dialog box
   - **Edit | Animate Analyzed Conformations** (if you activated a conformational analysis window) to display the Animate Analyzed Conformations dialog box

   The Animate Along Horizontal Axis dialog box, Animate All Conformations dialog box, and Animate Analyzed

Conformations dialog box function in an identical way. The Animate All Conformations dialog box is shown below.





3. Select the forward button, shown to the left, to animate your molecule.

   Depending on which type of window is active, one of the following occurs:

   - For a **graph window**, the conformation window steps through the conformations along the graph axis that is most closely aligned with the horizontal axis based on the graph's current rotation. (By rotating the graph you can control which axis is animated, and which is held constant.)
   - For a **conformation window**, the conformation window steps through each conformation in the map file.
   - For a **conformational analysis** window, the conformation window steps through each conformation listed in the conformational analysis window. The molecule in the conformation window moves through each variable value in turn to display the range of conformations. At the same time, the spherical marker in the graph window moves to each corresponding graph location.

   The **Conformation** text box in the relevant Animate dialog box displays the position of the current conformation in the range of conformations. The box to the right of the **Conformation** text box displays the total number of conformations in the range.



4. To stop the animation at a particular conformation, select the stop button, shown to the left.

   The molecule stops moving in the conformation window and the marker remains stationary in the graph window. The

Conformation text box in the relevant Animate dialog box displays the position of the current conformation in the range of conformations.



5. To animate your molecule from the last to the first conformation, select the reverse button, shown to the left.

   The molecule in the conformation window moves through each variable value to display the range of conformations in reverse order. At the same time, the spherical marker in the graph window moves in reverse order to each corresponding graph location.

6. To display a conformation in a particular location in the range, do one of the following:

   In the relevant Animate dialog box, select the up or down arrow buttons in the **Conformation** text box to increase or decrease the value displayed.

   In the relevant Animate dialog box, click in the **Conformation** text box and type the step number of the conformation you want to view.

   The conformation at the specified position in the range is displayed in the conformation window, and the spherical marker in the graph window displays the corresponding graph location.

7. To display a conformation with a particular variable value, do the following:

   In the graph window, conformation window, or conformational analysis window, select the arrow button in the left-hand parameter bar box and choose a variable from the drop-down list.

   Select the up or down arrow button in the right-hand parameter bar box to choose a value for the variable.

   The conformation with the specified variable value is displayed in the conformation window, and the spherical marker in the graph window displays the corresponding graph location.

8. To display a conformation in the conformational analysis list, double-click on the conformation in the list.

   A second conformation window opens, displaying the selected

conformation.

9. To view the first conformation in the map file range of conformations, select the rewind button, shown to the left, in the Animate Along Horizontal Axis, Animate All Conformations, or Animate Analyzed Conformations dialog box.



   The conformation window displays the first conformation in the range. The marker in the graph window moves to the beginning of the graph.

10. To view the last conformation in the range, select the forward button, shown to the left, in the Animate Along Horizontal Axis, Animate All Conformations, or Animate Analyzed Conformations dialog box.



    The conformation window displays the last conformation in the range. The marker in the graph window moves to the end of the graph.

11. To modify the range of steps by which you are animating the molecule, do one of the following:

    - Select the up or down arrow buttons in the **Step by** text box to increase or decrease the value displayed.
    - Click in the **Step by** text box in the Animate Along Horizontal Axis, Animate All Conformations, or Animate Analyzed Conformations dialog box, and enter the number of steps by which you want to animate the molecule.

12. To finish the animation, do one of the following:

    - Select **Done** in the relevant Animate dialog box to close the dialog box and to display the conformation at which you finished the animation in the conformation window.
    - Select **Cancel** to close the relevant Animate dialog box and to display the conformation you had prior to animating the map file.

Saving map files

CAChe offers two saving options that are specific to map files. You can save the following:

- the current conformation in the conformation window as a new chemical sample file
- selected conformations in a conformational analysis window as new chemical sample files. You can save one or more conformations from the conformational analysis window. Each conformation is saved into a separate chemical sample file.

To save a conformation in the conformation window as a chemical sample file

1. Activate the conformation window which displays the conformation that you want to save as a chemical sample file.
2. Choose **File | Save As Chemical Sample** to display the Save As dialog box.
3. Click in the **File name** text box and type the name of the new chemical sample file.
4. Select the arrow button in the **Save as type** box and choose **Chemical Sample (*.csf)** from the drop-down list.
5. Select **Save** to save the conformation in the chemical sample file and to close the Save As dialog box.

To save conformations in the conformational analysis window as chemical sample files

1. Select one or more conformations in a conformational analysis window by clicking on the conformations.
2. Choose **File | Save Selected Conformations As** to display the Save As dialog box.
3. Click in the **File name** text box and type the name of the new chemical sample file.

   The file name you enter will apply to all the files you are saving, with each file name appended with the number that corresponds

to that structure's place within the energy list. For example, `chem005.csf` would be the fifth lowest energy in the list.

4. Select the arrow button in the **Save as type** box and choose **Chemical Sample (*.csf)** from the drop-down list.
5. Select **Save** to save the conformations in separate chemical sample files and to close the Save As dialog box.

15 Investigating Electron Distribution

Overview

This chapter describes the various types of experiments that CAChe offers to predict electron distribution in your chemical sample, including experiments that generate:

- electron density surfaces
- electrostatic potential surfaces
- molecular orbital surfaces.

Contents

Investigating electron density surfaces 15-2
Generating electron density colored by electrostatic potential 15-3
Generating an electron density surface colored by susceptibility 15-4
Generating an electron density surface colored by superdelocalizability 15-5
Generating an electrostatic potential surface 15-6
Investigating molecular orbital energies 15-7
Calculating HOMO and LUMO energies 15-7
Calculating HOMO -5 to LUMO +4 energies 15-8
Calculating all molecular orbital energies 15-8
Viewing a surface 15-9
Hiding a surface 15-10
Interpreting surface color 15-11
CAChe color tables 15-13
Interpreting surfaces 15-15
Changing display options for surfaces 15-18

Investigating electron density surfaces

CAChe generates surfaces from the following experiments:

- electron density
- nucleophilic susceptibility
- electrophilic susceptibility
- radical susceptibility
- nucleophilic superdelocalizability
- electrophilic superdelocalizability
- radical superdelocalizability
- electrostatic potential
- HOMO and LUMO
- HOMO-5 to LUMO+4
- all molecular orbitals.

You can also use CAChe procedures for generating electron density surfaces to:

- optimize the geometry of the molecule first using classical mechanics, quantum mechanics, or a combination of both.

You can combine all optimization procedures with generating electron density for your sample.

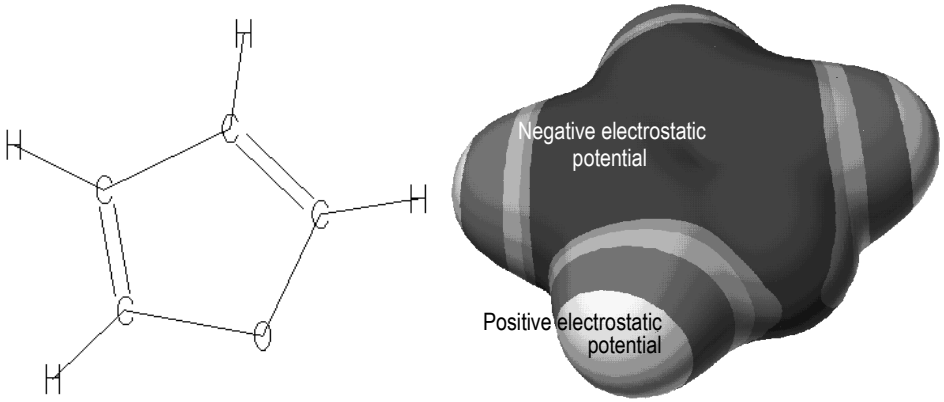
NOTE You cannot use procedures that involve MOPAC or ZINDO in Personal CAChe.

Generating electron density colored by electrostatic potential

You can generate an electron density surface colored by electrostatic potential to view charge distribution in a molecule. The three-dimensional electron density isosurface that is produced gives a more accurate representation of the true shape of your chemical sample.

An electron density isosurface for an electron probability density of 0.01 e-/Å3 is generated. This surface is colored to reflect the electrostatic potential at every point on the surface. Surface color changes to reflect the magnitude and polarity of the electrostatic potential.

The following example shows a line drawing of a furan molecule, and an electron density surface for the same molecule, colored to show electrostatic potential, which indicates furan's charge distribution.



The colors displayed depend on the current colors assigned to each of the color indexes.

Refer to *"CAChe color tables"*, p 15-13, for details about assigned colors.

Generating an electron density surface colored by susceptibility

You can generate an electron density surface colored by:

- nucleophilic susceptibility
- electrophilic susceptibility
- radical susceptibility.

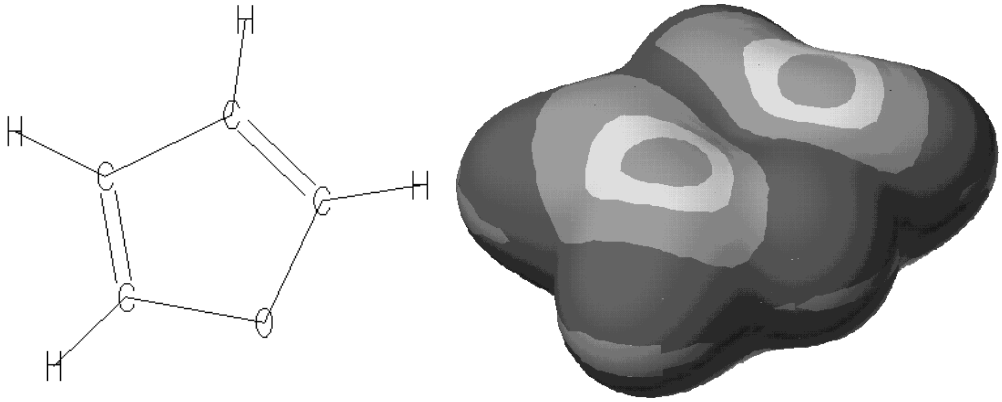
Susceptibility provides clues about which parts of your chemical sample are vulnerable to an attack by three different type of species: electrophiles, nucleophiles, and radicals.

After an optimization step, the electron distribution of orbitals near your sample's frontier orbitals (molecular orbitals near the highest occupied molecular orbital or HOMO and lowest unoccupied molecular orbital or LUMO) are evaluated.

A three-dimensional electron density isosurface is created that can be superimposed over your chemical sample. Shape and color give you clues to the relative reactivity of different sites. Reactive centers can be easily identified as the centers of brightly colored "bullseye" patterns on the isosurface.

📖 NOTE Susceptibility and superdelocalizability experiments (described in the next section) give similar results, but susceptibility experiments are recommended because they are widely applicable.

The following example shows a line drawing of a furan molecule, and an electron density surface for the same molecule, colored to show susceptibility to attack by an electrophile.



Generating an electron density surface colored by superdelocalizability

You can generate an electron density surface colored by:

- nucleophilic superdelocalizability
- electrophilic superdelocalizability
- radical superdelocalizability.

Superdelocalizability is similar to susceptibility, but is more sensitive to the relationship between the frontier orbital energies of your chemical sample versus any specific electrophilic, nucleophilic, or radical species that would be reacting with your sample.

In most cases, susceptibility yields similar results without dependencies on reagent energies. Superdelocalizability output is a three-dimensional electron density isosurface with colors reflecting the relative differences in reactivity of the different parts of your sample.

Superdelocalizability experiments produce more accurate results in the following conditions:

- your sample's HOMO energy is less than the default energy of -8eV for electrophilic superdelocalizability, -2eV for nucleophilic superdelocalizability, and -5eV for radical superdelocalizability
- your sample's LUMO energy is greater than the default energy of -8eV for electrophilic superdelocalizability, -2eV for nucleophilic superdelocalizability, and -5eV for radical superdelocalizability
- the energies of the attacking molecule's frontier orbitals are between the HOMO and LUMO energies of your sample.



Refer to *"Investigating molecular orbital energies"*, p 15-7, for information on how to perform a frontier orbitals experiment to determine HOMO and LUMO energies for your chemical sample, and the attacking reagent molecule.

Generating an electrostatic potential surface

CAChe investigates the electrostatic potential of a sample by generating an electronic wavefunction using a quantum mechanics computational application and using the data to create a three-dimensional surface.

An electrostatic potential isosurface is created that shows both the polarity of the potential and where in space the potential equals ±0.03 a.u. (±18 Kcals/mol, ±75 kJ/mol). An electrostatic potential surface is particularly useful if you are interested in the reactivity of your sample to a charged or polar reactant.

CAChe procedures for generating an electrostatic potential surface also enable you to:

- optimize the geometry of the molecule first using classical mechanics, quantum mechanics, or a combination of both.

You can combine all optimization procedures with generating electron density for your sample.

📖 NOTE You cannot use procedures that involve MOPAC or ZINDO in Personal CAChe.

Investigating molecular orbital energies

The following three experiments calculate the energies and shapes of your sample's molecular orbitals by generating an electronic wavefunction in a quantum mechanical computational application:

- HOMO and LUMO
- HOMO -5 to LUMO +4
- all molecular orbitals.

CAChe procedures for calculating molecular orbital energies also enable you to:

- optimize the geometry of the molecule first using classical mechanics, quantum mechanics, or a combination of both.

You can combine all optimization procedures with generating electron density for your sample.

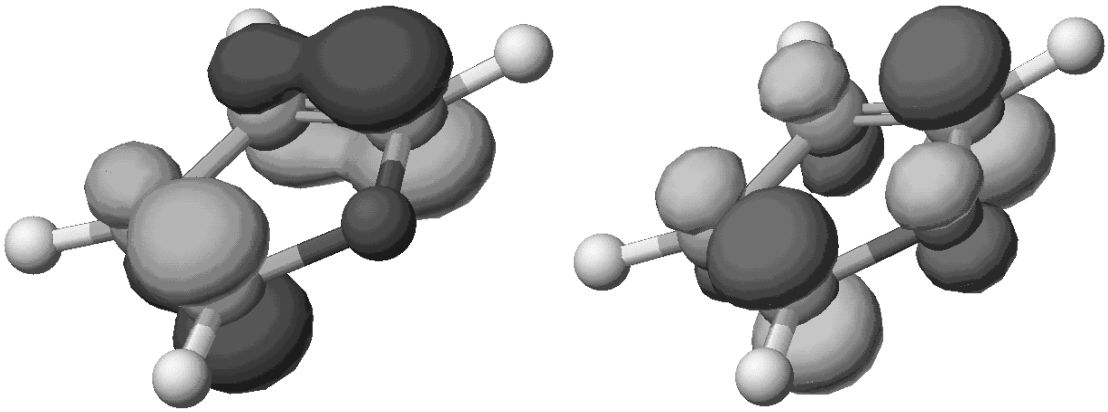
📖 NOTE You cannot use procedures that involve MOPAC or ZINDO in Personal CAChe.

Calculating HOMO and LUMO energies

A HOMO and LUMO experiment uses a quantum mechanical application to generate an electronic wavefunction and calculate the energies and shape of the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) of your chemical sample.

The energy of the HOMO is the energy required to remove an electron from the HOMO (ionization energy), and the energy of the LUMO is the energy added to the sample when an electron is added to the LUMO (electron affinity).

The following example shows calculated HOMO and LUMO energies for a furan molecule, colored to show electrostatic potential, which indicates furan's charge distribution.



HOMO energies LUMO energies

Calculating HOMO -5 to LUMO +4 energies

This experiment is similar to the HOMO and LUMO experiment described in the previous section. The difference is that a total of nine molecular orbitals are generated, ranging from HOMO -5 to LUMO +4.

Often, large molecules have several orbitals clustered near the HOMO and LUMO. Viewing the shapes and energies of these orbitals can be useful.

Calculating all molecular orbital energies

This experiment calculates the shapes and energies of all of the molecular orbitals in your chemical sample. Choose this experiment when the orbitals you are interested in lie outside the HOMO -5 to LUMO +4 range.

Do not use this experiment without careful consideration, simply because it requires a significant amount of disk space to store all the orbitals for large molecules.

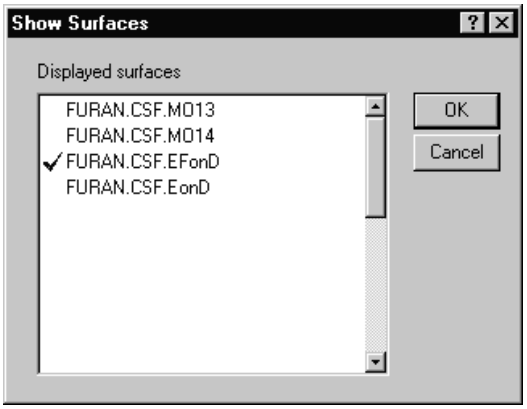
Viewing a surface

When you run an experiment that generates a surface for your molecule, a surface file (`*.iso`) is created, which contains information that CAChe uses to build a three-dimensional molecular surface representing electronic properties. You view this shaded surface superimposed on your molecule in the chemical sample file. You do not open the isosurface file to view the surface.

To display a surface

1. Choose **File** | **Open** to display the Open dialog box.
2. Double-click on the `Cache` folder to open it.
3. Select the arrow button in the **Files of type** box and choose **Chemical sample (*.csf)** from the drop-down list.
4. Click and drag on the scroll bar of the scrolling list to locate the relevant chemical sample file for which you generated the surface.
5. Double-click on the required chemical sample file to open it.

   The chemical sample file opens.
6. Choose **Analyze** | **Show Surfaces** to display the Show Surfaces dialog box.



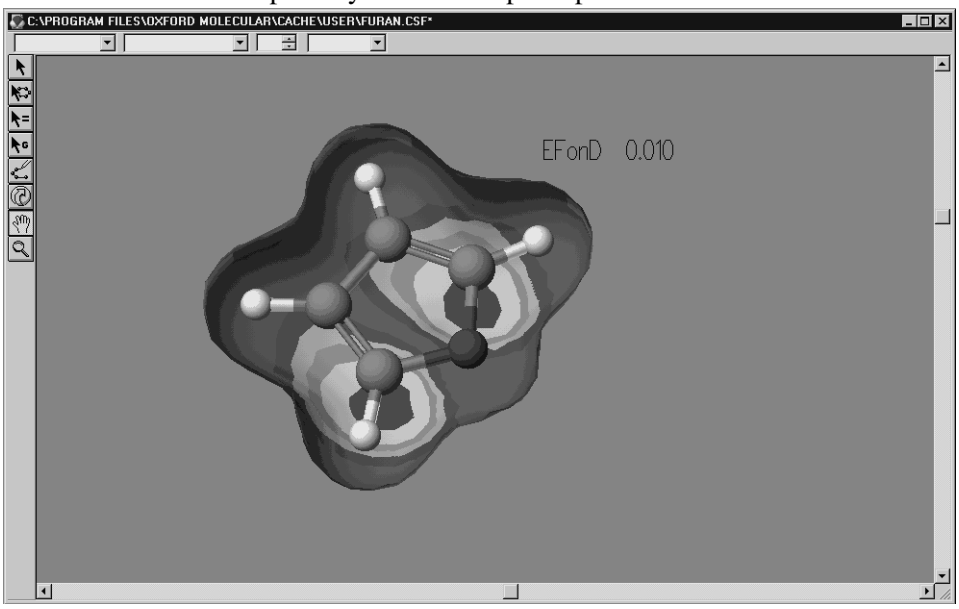
The Show Surfaces dialog box lists all the surfaces generated for the chemical sample file.

7. Select one or more surfaces by clicking on the required surfaces in the **Displayed surfaces** list.

   A check mark is displayed next to the selected surfaces.

8. Select **OK** to close the Show Surfaces dialog box.

   CAChe processes surface information for the chemical sample and displays the surface superimposed on the molecule in the workspace. The example below shows electrophilic susceptibility for furan superimposed on a furan molecule.



Hiding a surface

You can hide surfaces individually, or choose to hide all surfaces in a chemical sample file.

To hide surfaces individually

1. Choose **Analyze** | **Show Surfaces** to display the Show Surfaces dialog box.

   All surfaces currently displayed in the chemical sample file are shown in the **Displayed surfaces** list with a check mark next to the surface name.

2. Select the surface that you want to hide by clicking on it in the **Displayed surfaces** list.

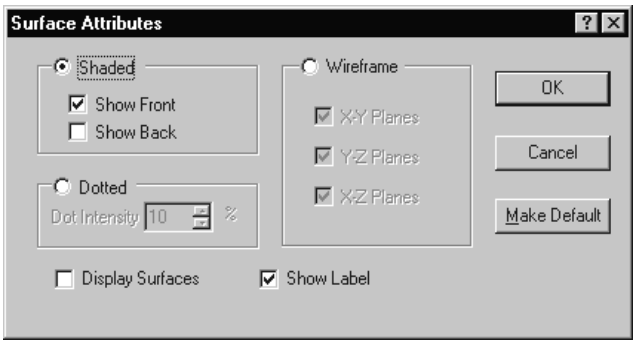
   The check mark is no longer displayed next to the surface name.

3. Select **OK** to close the Show Surfaces dialog box.

   The selected surface is no longer displayed in the workspace.

To hide all surfaces

1. Choose **Analyze** | **Surface Attributes** to display the Surface Attributes dialog box.



2. Select the **Display Surfaces** check box so that it is disabled.
3. Select **OK** to hide all surfaces in the chemical sample file and to close the Surface Attributes dialog box.

   Surfaces are no longer displayed in the workspace.

Interpreting surface color

Electron density, susceptibility, and superdelocalizability experiments all generate electron density isosurfaces with colors representing a second chemical property. The transition from one color to another occurs at a threshold value. You can view the actual value associated with each color transition for a surface, as described in the next section, *"Viewing color threshold values"*.

The use of color in other surface experiments such as investigating electrostatic potential and generating molecular orbitals is explained in the section *"CAChe color tables"*, p 15-13.

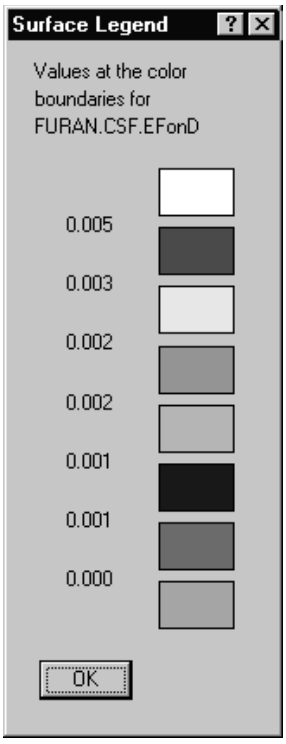
Viewing color threshold values

To view values associated with surface color thresholds

1. Select a surface by clicking on its label with the Select tool.

   The surface is highlighted in the workspace to show that it is selected.

2. Choose **Analyze** | **Surface Legend** to display the Surface Legend dialog box.



The Surface Legend dialog box displays the threshold value of transition from one surface color to another for the selected surface. The colors displayed depend on the current colors assigned to each of the color indexes listed in the following CAChe color tables.

NOTE Any color indexes you selected previously using the **View** | **Color Palette** option will replace the default colors.

CAChe color tables

The following tables list colors and color index values for properties calculated by CAChe experiments. The colors listed are the default colors present when you install the software. If you have changed colors using the color palette, only the indexes in the table below will be accurate.

You can reset colors to the default values by deleting the `cache.ini` file, located in the same folder as `cache.exe`. Deleting `cache.ini` returns all CAChe defaults to their original settings.

Electron density surfaces

The following applies to electron density surfaces colored by electrostatic potential, superdelocalizability, or susceptibility.

Color index	Color, RGB values	Relative value of surface property
1	White, 255, 255, 255	Highest
2	Gray, 150, 150, 150	
3	Red, 255, 0, 51	
4	Yellow, 255, 255, 51	
5	Green, 0, 255, 0	
6	Blue, 51, 51, 255	
7	Purple, 255, 0, 255	
8	Cyan, 0, 255, 255	Lowest

Electrostatic potential polarity

Color index	Color, RGB values	Electrostatic potential and occupied MO polarity
3	Red, 255, 0, 51	Positive
6	Blue, 51, 51, 255	Negative

Occupied molecular orbital polarity

Color index	Color, RGB values	Electrostatic potential and occupied MO polarity
6	Blue, 51, 51, 255	Positive
5	Green, 0, 255, 0	Negative

Partial charge and unoccupied molecular orbital polarity

Color index	Color, RGB values	Partial charge and unoccupied MO polarity
3	Red, 255, 0, 51	Positive
4	Yellow, 255, 255, 51	Negative

Bond strain

Color index	Color, RGB values	Bond strain (kJ/mole)
6	Blue, 51, 51, 255	0 - 0.99
5	Green, 0, 255, 0	1 - 9.99

Color index	Color, RGB values	Bond strain (kJ/mole)
4	Yellow, 255, 255, 51	10 - 99.99
3	Red, 255, 0, 51	100 - 999.99

Bond order and bond type

Color index	Color, RGB values	Bond order, type
5	Green, 0, 255, 0	0 - 0.60, Weak
3	Red, 255, 0, 51	0.61 - 1.60, Single
4	Yellow, 255, 255, 51	1.61 - 2.60, Double
8	Cyan, 0, 255, 255	>2.60, Triple
1	White, 255, 255, 255	Ionic
7	Purple, 255, 0, 255	Coordination

Interpreting surfaces

The following section describes how to interpret the appearance of the three-dimensional surfaces that CAChe produces for different types of experiment.

Electron density surfaces

Surface files that represent electron density properties are referred to as isosurface files, depicting locations around your sample where the electron probability density is equal. The electron density at the surface is 0.01 e/Å^3.

Although the electron density surface by itself is useful, CAChe adds another property on top of it. The electrostatic potential of your sample is calculated and added to the electron density surface as color.

Along the electron isodensity surface, different magnitudes of electrostatic potential are represented by different colors. The colors displayed depend on the current colors assigned to each of the color indexes listed in the earlier color tables.

Susceptibility and frontier density

All three of the frontier density experiments (nucleophilic, electrophilic, and radical) generate an electron density surface similar to the electron density experiment.

However, the surface colors represent reactivity based on active orbitals near the frontier orbitals (HOMO and LUMO).

In the frontier density surface, locations in your chemical sample that are susceptible to attack (nucleophilic, electrophilic, or free radical) are identified by bright bull's eye patterns. The remainder of the surface is colored to indicate the relative reactivity towards attack.

Use the Surface Legend dialog box, accessed by choosing **Analyze | Surface Legend**, to determine the reactivity represented by each color. The colors corresponding to larger values in the surface legend represent more reactive sites.

Superdelocalizability

Each of the three superdelocalizability experiments (electrophilic, nucleophilic, and radical) generates an electron isodensity surface. The surface colors represent reactivity based on active orbitals near the frontier orbitals (HOMO and LUMO).

The nucleophilic experiment creates an electron density isosurface with colors reflecting the relative reactivity of your sample to a nucleophilic reagent. Similarly, the electrophilic and radical superdelocalizability routines build surfaces that show where an electrophile or a radical has the highest probability of initiating a reaction.

Use the Surface Legend dialog box, accessed by choosing **Analyze | Surface Legend**, to determine the reactivity represented by each color. The colors corresponding to larger values in the surface legend represent more reactive sites.

Susceptibility (frontier density) and superdelocalizability are similar, and so are the surfaces they generate. However, susceptibility experiments and surfaces yield more accurate results for a wider range of chemical samples.

Superdelocalizability experiments produce more accurate results in the following conditions:

- your sample's HOMO energy is less than the default energy of -8eV for electrophilic superdelocalizability, -2eV for nucleophilic superdelocalizability, and -5eV for radical superdelocalizability
- your sample's LUMO energy is greater than the default energy of -8eV for electrophilic superdelocalizability, -2eV for nucleophilic superdelocalizability, and -5eV for radical superdelocalizability
- the energies of the attacking molecule's frontier orbitals are between the HOMO and LUMO energies of your sample.

Molecular orbitals

There are three different experiments that produce molecular orbital surface files:

- HOMO and LUMO
- HOMO-5 to LUMO+4
- all molecular orbitals.

The HOMO and LUMO experiment creates only two surface files, one for your sample's highest occupied molecular orbital (HOMO) and one for its lowest unoccupied molecular orbital (LUMO). Since these two orbitals often determine your sample's reactivity, this experiment can be quite useful. Note that if there are degenerate HOMOs or LUMOs, all will be generated.

The HOMO-5 to LUMO+4 experiment generates a total of eleven orbital surfaces, if your sample has that many, including the HOMO and LUMO.

The all molecular orbitals experiment calculates isosurfaces for all of your sample's molecular orbitals.

The MO surface files created by all three of these experiments depict surfaces with an electron probability amplitude of 0.07 a.u. The default molecular orbital colors for occupied orbitals are green and blue and the defaults for unoccupied orbitals are red and yellow.

Color assignment with respect to positive and negative phase is arbitrary, so identical calculations can result in surfaces with opposite colors. You can switch these colors using the color palette, accessed by choosing **View | Color Palette**. If you change green and blue in the color palette to two different colors, the occupied orbital surfaces are displayed in the nearest colors to green and blue.

You can open the surfaces of several molecular orbitals at the same time by choosing **Analyze | Show Surfaces**.

Electrostatic potential

An electrostatic potential surface represents the distance from your sample at which a proton experiences a set attraction or repulsion. The value of the electrostatic potential on the surface is ±0.03 a.u. (±18 kCals/mol, ±75 kJ/mol).

Electrostatic potential is normally represented by red and blue to indicate positive and negative potential, respectively. You can switch these colors using the color palette, accessed by choosing **View | Color Palette**.

Changing display options for surfaces

You can choose whether to display surfaces as:

- shaded three-dimensional surfaces
- dotted three-dimensional surfaces
- wireframe three-dimensional surfaces
- labeled or unlabeled.

Viewing shaded surfaces

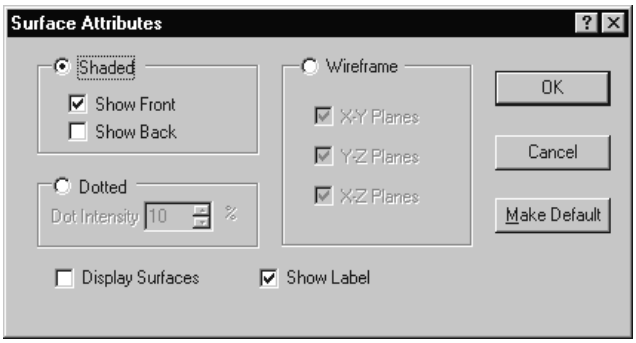
When viewing surfaces as shaded and solid, you have the option of viewing:

- the front of the surface only, which displays the portion of the surface facing you
- the back of the surface only, which displays the back of the surface as a shell in which the molecule is floating.

Displaying surfaces as shaded is the default view option.

To display shaded surfaces

1. Select a surface by clicking on its label with the Select tool.
2. Choose **Analyze | Surface Attributes** to display the Surface Attributes dialog box.



3. Select the **Shaded** radio button so that it is enabled.
4. Do one of the following:
   - To display the front of the surface, select the **Show Front** check box so that it is enabled.
   - To display the back of the surface, select the **Show Back** check box so that it is enabled.
5. Select **OK** to view the selected surface as the front or back of a solid shaded surface, and to close the Surface Attributes dialog box.

Viewing dotted surfaces

When viewing surfaces as dotted, you can choose the density of the surface rendering.

To display dotted surfaces

1. Select a surface by clicking on its label with the Select tool.
2. Choose **Analyze | Surface Attributes** to display the Surface Attributes dialog box.
3. Select the **Dotted** radio button so that it is enabled.
4. Do one of the following:
   - Select the up or down arrow button in the **Dot Intensity** text box to increase the dot intensity to a maximum of `9`.
   - Click in the **Dot Intensity** text box and type an integer between `1` and `9`.

Viewing wireframe surfaces

When viewing surfaces as wireframe, you have the option of viewing only the portion of the wireframe which is parallel to:

- the x, y plane of your chemical sample
- the y, z plane of your chemical sample
- the x, z plane of your chemical sample.

To display wireframe surfaces

1. Select a surface by clicking on its label with the Select tool.
2. Choose **Analyze | Surface Attributes** to display the Surface Attributes dialog box.
3. Select the **Wireframe** radio button so that it is enabled.
4. To view the portion of the wireframe which is parallel to the x, y plane, select the **X-Y Planes** check box so that it is enabled.
5. To view the portion of the wireframe which is parallel to the x, y plane, select the **Y-Z Planes** check box so that it is enabled.

6. To view the portion of the wireframe which is parallel to the x, y plane, select the **X-Z Planes** check box so that it is enabled.

Viewing labeled surfaces

If you have many surfaces displayed at one time, you may find several labels cluttering up the workspace.

Displaying surface labels is useful for selecting a surface and for viewing the name of a surface. Displaying surfaces as labeled is the default view option.

To view a surface label

1. Do one of the following to select everything in the workspace:
   - Choose **Edit** | **Select All**.
   - Press **Ctrl A**.
   - Click anywhere in the workspace background.

   Every object in the workspace is highlighted to show that it is selected.
2. Choose **Analyze** | **Surface Attributes** to display the Surface Attributes dialog box.
3. Select the **Show Label** check box so that it is enabled.
4. Select **OK** to show labels for all surfaces currently being displayed and to close the Surface Attributes dialog box.

   All surfaces in the workspace are now labeled.

To hide a surface label

1. Select a surface by clicking on its label with the Select tool.

   The surface is highlighted to show that it is selected.
2. Choose **Analyze** | **Surface Attributes** to display the Surface Attributes dialog box.
3. Select the **Show Label** check box so that it is disabled.
4. Select **OK** to hide labels for all currently selected surfaces and to close the Surface Attributes dialog box.

   All surfaces in the workspace are no longer labeled.

16 Investigating Atom and Bond Properties

Overview

This chapter describes the following CAChe experiments that calculate atom and bond properties:

- the atomic partial charge experiment, which displays a chemical sample with atoms sized to reflect their partial charge, and enables you to view possible reactivity sites and the most polar bonds in a sample
- the bond order experiment, which displays a chemical sample with bonds scaled or colored to reflect calculated bond order
- the bond strain experiment, which displays a chemical sample with bond strain represented by colors that indicate the order of magnitude of the strain energy.

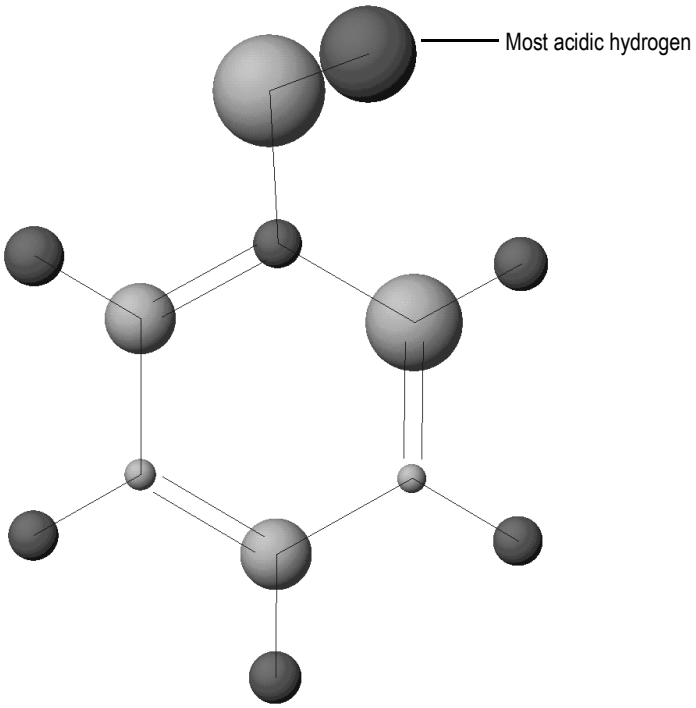
Contents

Calculating atomic partial charge 16-2
Calculating bond properties 16-4
Calculating bond order 16-4
Calculating bond strain 16-5
Viewing atom and bond properties 16-7
Displaying partial charge and bond order 16-7
Displaying partial charge with labeled atoms 16-8
Displaying partial charge with scaled and colored atoms 16-10
Displaying bond order and partial charge 16-11
Displaying bond order with color 16-11
Displaying bond order by scaling bond radius 16-12
Displaying bond strain 16-13

Calculating atomic partial charge

Quantum mechanical methods are used to optimize the sample and determine the partial charge for all atoms. Both partial charge and bond order are calculated at the same time, so you do not need to run separate experiments to get both properties.

After you run a partial charge experiment, you can choose to view your chemical sample with atoms sized to reflect their partial charge. This enables you to view possible reactivity sites more clearly, and shows you which bonds in your sample are most polar. The example below shows phenol with atoms sized to reflect partial charge.



If you know the partial charges on atoms in two reagents, you have a good idea about which part of each molecule is likely to interact. You can also view the relative acidity of different hydrogens more clearly, because the largest positive partial charge is likely to be the most acidic.

If you have run an experiment that employed a quantum mechanical procedure previously, this information is already present in the chemical sample file and you do not need to re-compute it unless you have changed the geometry of the molecule.

CAChe procedures for calculating atomic partial charge also enable you to:

- optimize the geometry of the molecule first using classical mechanics, quantum mechanics, or a combination of both.

You can combine all of the optimization procedures with calculating atomic partial charge for your sample.

📖 NOTE You cannot use procedures that involve MOPAC or ZINDO with Personal CAChe.

Calculating bond properties

CAChe offers the following bond property experiments:

- calculated bond order
- calculated bond strain.

Calculating bond order

You can calculate bond order using one of the quantum mechanical applications. CAChe determines the experimental bond order of each bond in your chemical sample. Both bond order and partial charge are calculated at the same time, so you do not need to run separate experiments to get both properties.

If you have run an experiment that employed a quantum mechanical procedure previously, this information is already present in the chemical sample file and you do not need to re-compute it unless you have changed the geometry of the molecule.

CAChe procedures for calculating bond order also enable you to:

- optimize the geometry of the molecule first using classical mechanics, quantum mechanics, or a combination of both.

You can combine all of the optimization procedures with calculating bond order for your sample.

📖 NOTE You cannot use procedures that involve MOPAC or ZINDO with Personal CAChe.

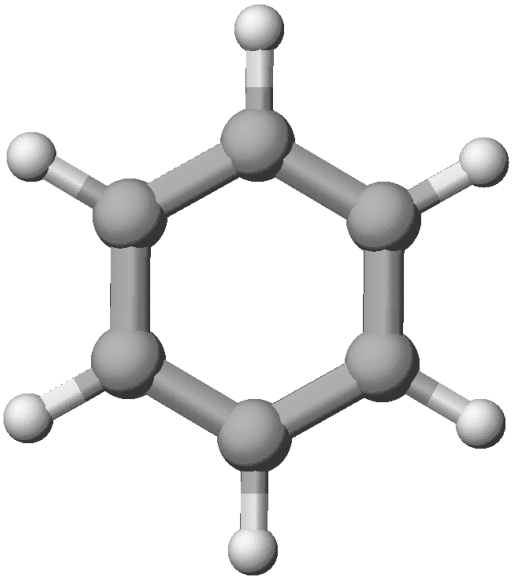
After you run a calculated bond order experiment, you can view bonds that are scaled to reflect calculated bond order. You can change the display ratio of a bond order of one to your choice of measurement in Angstroms.

Many models use alternating single and double bonds (resonance structures) to represent delocalized π electrons in rings. For example, in benzene, all of the C-C bonds are the same length. This could not be the case if half the bonds are double, and half are single.

Calculating bond order using a CAChe experiment and displaying the results by scaling bond cylinders by calculated bond order shows

that all the C-C bond orders are equal and greater than the C-H bond orders. The cylinders between carbons are roughly one and a half times thicker than those between carbons and hydrogens, illustrating the bond order of 1.5.

The following example shows a benzene molecule with bonds sized to reflect calculated bond orders.



Calculating bond strain

Bond strain is a purely classical mechanical quantity, calculated every time a classical mechanical calculation is performed. As a result, this property is often a subset of the results when you experiment with other properties.

CAChe examines bond angles and atom distances in your molecule and compares the geometry to the classical mechanical ideal value. Deviations from the ideal accumulate a relative energy quantity known as steric or potential energy.

CAChe calculates these deviations from the ideal to discover bond strain.

After you run a bond strain experiment, you can display bond strain represented by colors that indicate the order of magnitude of the

strain energy. Tension and compression can both lead to strain and are indistinguishable. For example, red indicates a high bond strain value and is indicative of a structure that has high potential (or steric) energy.



Refer to *"CAChe color tables"*, p 15-13, for details of the bond strain colors and energy values they represent.

Viewing atom and bond properties

After you run a partial charge or bond order experiment, you can view atomic partial charge in your chemical sample file by choosing a CAChe modeling style, or customizing the display of partial charge, using one of the following two view options:

- atoms labeled with partial charge
- atoms sized and colored to reflect partial charge.

Similarly, you can view bond order in your chemical sample file by choosing a CAChe modeling style, or customizing display of bond order, by choosing one of the following two view options:

- bonds colored by bond order
- scale the radius of bonds by bond order.

When bonds are colored by bond order, CAChe determines which of the standard bond types is closest to the bond order of each bond in your sample. A calculated bond order of 1.5 is rounded to 1.0, and is colored red, the default color of a single bond. Because there are no colors for fractional bond orders, it is often useful to display bond order by both color and by scaling bond radius.

Displaying partial charge and bond order

To view atomic partial charge and calculated bond order

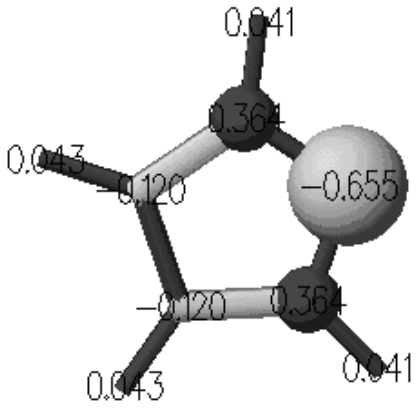
1. Run an atomic partial charge or calculated bond order experiment on your chemical sample file.
2. Choose **View | Partial Chg and Calc. Bond Order**.

   CAChe colors atoms by partial charge polarity where positively charged atoms are red and negatively charged atoms are yellow. Atoms are also labeled with partial charge and scaled to reflect partial charge.

   Bonds are colored by calculated bond order, according to the CAChe color tables.

   The following example shows a furan molecule viewed by

partial charge and calculated bond order.

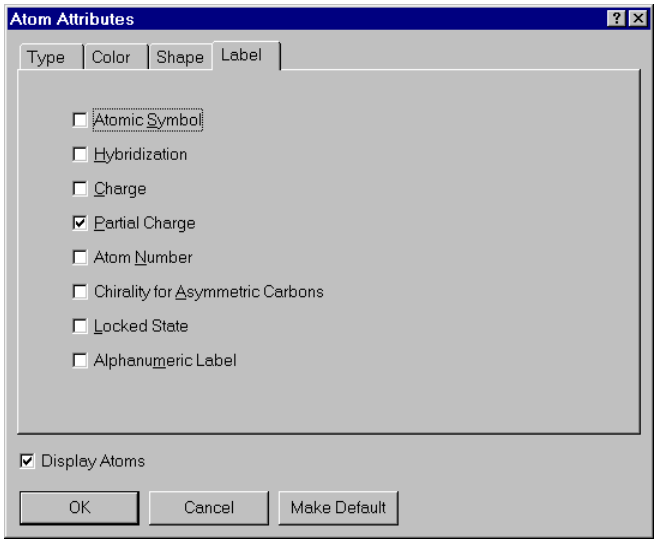


Refer to *"CAChe color tables"*, p 15-13, for further details about bond colors.

Displaying partial charge with labeled atoms

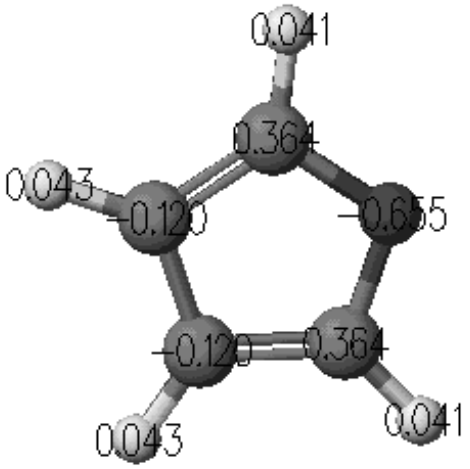
To view atoms labeled with partial charge

1. Run an atomic partial charge or calculated bond order experiment on your chemical sample file.
2. Choose **View | Atom Attributes** to display the Atom Attributes dialog box.



3. Select the **Label** tab to display a list of labeling options for atoms.
4. Select the **Partial Charge** check box so that it is enabled.
5. Select **OK** to close the Atom Attributes dialog box.

   Atoms in the workspace are labeled with partial charge, as shown in the following example.

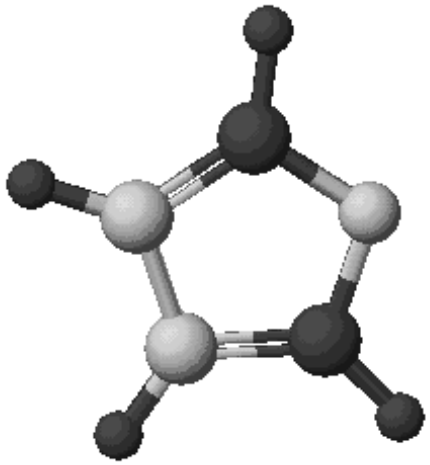


Displaying partial charge with scaled and colored atoms

To view partial charge with scaled and colored atoms

1. Run an atomic partial charge or calculated bond order experiment on your chemical sample file.
2. Choose **View | Atom Attributes** to display the Atom Attributes dialog box.
3. Select the **Color** tab to display a list of labeling options for atoms.
4. Select the **Partial Charge Polarity (+/-)** check box so that it is enabled.
5. Select **OK** to close the Atom Attributes dialog box.

   Atoms in the workspace are colored by partial charge polarity, where positively charged atoms are displayed on screen in red and negatively charged atoms are displayed on screen in yellow, as shown in the following example.



Displaying bond order and partial charge

To view atomic partial charge and calculated bond order

1. Run an atomic partial charge or calculated bond order experiment on your chemical sample file.
2. Choose **View | Partial Chg and Calc. Bond Order**.

   CAChe colors atoms by partial charge polarity where positively charged atoms are red and negatively charged atoms are yellow. Atoms are also labeled with partial charge and scaled to reflect partial charge.

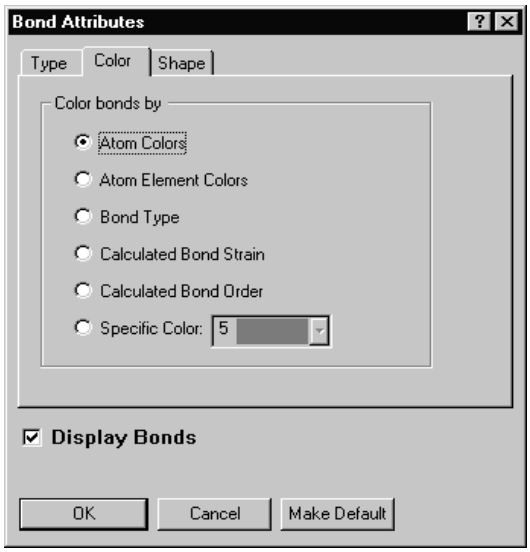
   Bonds are colored by calculated bond order, according to the CAChe color tables.

Refer to *"CAChe color tables"*, p 15-13, for further details about bond colors.

Displaying bond order with color

To view bond order with colored bonds

1. Run an atomic partial charge or calculated bond order experiment on your chemical sample file.
2. Choose **View | Bond Attributes** to display the Bond Attributes dialog box.



3. Select the **Color** tab to display a list of color options for bonds.
4. Select the **Calculated Bond Order** radio button so that it is enabled.
5. Select **OK** to close the Bond Attributes dialog box.

   Bonds are colored to reflect bond order, according to the CAChe color tables.

Refer to *"CAChe color tables"*, p 15-13, for further details about bond colors.

Displaying bond order by scaling bond radius

To view bond order by scaled bond radius

1. Run an atomic partial charge or calculated bond order experiment on your chemical sample file.
2. Choose **View** | **Bond Attributes** to display the Bond Attributes dialog box.
3. Select the **Shape** tab to display a list of shape options for bonds.

4. Select the arrow button in the **Scale cylinders such that** box and choose **Formal Bond Order of 1** from the drop-down list.
5. Click in the **is displayed as** text box and type a value for the radius to which bonds with a formal bond order of 1 will be scaled. The value must be between `0.001` and `0.999`.
6. Select **OK** to close the Bond Attributes dialog box.

   Bonds are scaled to the specified radius.

Displaying bond strain

To view bond strain

1. Run a bond strain experiment on your chemical sample file.
2. Choose **View | Bond Attributes** to display the Bond Attributes dialog box.
3. Select the **Color** tab to display a list of color options for bonds.
4. Select the **Calculated Bond Strain** radio button so that it is enabled.
5. Select **OK** to close the Bond Attributes dialog box.

   Bonds are colored to reflect bond strain, according to the CAChe color tables.

Refer to *"CAChe color tables"*, p 15-13, for further details about bond colors.

17 Investigating Reactions

Overview

This chapter describes the CAChe experiments that investigate the conformations of your molecule during a chemical reaction, including the following transition state experiments:

- search for saddle, which generates a transition state structure
- refine transition, which refines a transition state structure using a minimize gradient calculation
- verify transition, which calculates the molecule's vibrational transitions to verify the transition state geometry.

The following reaction path experiment is also described:

- map reaction, which produces an optimized energy map by varying one or two search labels and measuring the energy of each resulting conformation using quantum mechanics
- find reaction paths, which generates structures in a reaction that your chemical sample will pass through as it proceeds from a transition state geometry to either the product or reactant side of the reaction pathway.

Contents

Investigating transition state structures 17-2
Viewing transition state structures 17-3
Investigating reaction path structures 17-4
Viewing reaction path structures 17-5

Investigating transition state structures

CAChe uses quantum mechanics to investigate transition state structures in a reaction path from a reactant molecule to a product molecule. The following types of experiment are available:

- search for saddle experiment
- refine transition state experiment
- verify transition state experiment.

The search for saddle experiment locates a stationary point between the reactant and product that corresponds to the transition state for the reaction. A stationary point is a structure where small geometry changes do not affect overall molecular energy.

Before generating a transition state structure, you must specify a reactant molecule and a product molecule (two chemical sample files) for input. The product molecule must have all the atoms of the reactant molecule, and each atom must have the same atom number. The only differences between reactant and product that are allowed are positions of atoms and bonds.

Once you have generated a transition state structure, you can refine it using a minimize gradient calculation in the refine transition state experiment.

You can then calculate the molecule's vibrational transitions to verify the current transition state geometry using the verify transition state experiment. A single negative vibration confirms a true transition state.

CAChe also allows you to include water solvent effects in a transition state experiment.

Refer to *"Modeling solvent effects with COSMO"*, p 20-19, for more information on experimental procedures that include solvation effects.

NOTE Transition state experiments are not available with Personal CAChe and BioCAChe.

Before running a search for saddle experiment

Because the reactant and product molecules must have all the same atoms and each atom must have the same atom number, the best way to prepare the two chemical sample files is to:

1. Save a copy of the reactant molecule.
2. Change the atom and bond positions to create the product molecule.
3. Save the file and use it as the product molecule.

   It is sometimes useful to specify a molecule structure for the product that is very close to the expected transition state structure.

Viewing transition state structures

The transition state structure resulting from a search for saddle experiment is saved in the chemical sample file of the reactant product. For this reason it is important to save a copy of the reactant chemical sample file before proceeding with a search for saddle experiment.

The contents of the product input file are untouched.

The resulting transition state structure from a refine transition state experiment is saved automatically in the chemical sample file on which the experiment was performed.

The resulting transition state structure from a verify transition state experiment is also saved automatically in the chemical sample file.

📖 TIP It is important to use the same parameter set and solvent effects when generating, refining, and verifying a transition state structure. For example, if you originally used AM1 parameters including the effect of water in your transition state experiment, use the same procedure when refining and verifying your transition state structure.

Investigating reaction path structures

CAChe calculates structures in a reaction that a chemical sample will pass through as it proceeds from a transition state geometry to either the product or reactant side of the reaction pathway. The reaction pathway is the minimum energy path from reactant to transition state structure to product. The following types of experiment are available:

- find reaction paths experiment
- map reaction experiment.

In a find reaction paths experiment, CAChe varies two internal coordinates of your chemical sample to form the principal deformations that occur in the course of a reaction. A series of reaction path structures are then calculated between the transition state structure to either the product or the reactant.

You can specify the direction for the reaction path calculation by choosing a vibrational mode for the initial motion of 1 or -1. The direction is purely arbitrary, except for the fact that the 1 and -1 modes are in opposite directions.

When generating reaction path conformations, you can:

- annihilate the kinetic energy of the molecule at every step using an IRC (Intrinsic Reaction Coordinate) calculation. Potential energy changes from conformation to conformation, and the resulting kinetic energy is annihilated so that the potential and total energies are the same.
- conserve the kinetic energy of the molecule at every step using a DRC (Dynamic Reaction Coordinate) calculation. Kinetic energy increases as potential energy is lost from conformation to conformation, so that total energy is constant.

The energy of each conformation is plotted in a separate map file where you can view the energy graph alongside each reaction path structure.

Start a find reaction paths experiment with a transition state structure generated by a search for saddle experiment.



Refer to *"Investigating transition state structures"*, p 17-2, for further details about generating a transition state structure.

You can also perform a map reaction experiment, which produces an optimized energy map by varying one or two search labels and measuring the energy of each resulting conformation using quantum mechanics.

📖 NOTE Reaction path experiments are not available with Personal CAChe and BioCAChe.

Viewing reaction path structures

Both a find reaction paths experiment and a map reaction experiment produce an energy map file, which you can view in the same way as any other map file.



Refer to *"Viewing map files"*, p 14-12, for further details about viewing map files.

18 Investigating Spectra

Overview

This chapter explains how to perform CAChe experiments to generate and view:

- infrared (vibrational) spectra
- UV-visible (electronic) spectra.

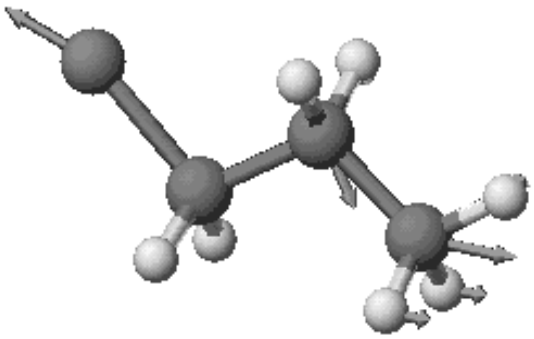
Contents

Investigating infrared spectra **18-2**
Viewing infrared spectra 18-2
Investigating UV-visible spectra **18-6**
Viewing UV-visible spectra 18-7

Investigating infrared spectra

CAChe enables you to view vibrational spectra for a molecule, created by coordinated motions of the atoms as electromagnetic radiation in the infrared (IR) region is absorbed by the molecule. Absorption bands observed in the infrared are associated with the bending and stretching of particular types of bonds, so viewing these infrared transitions aids the analysis of molecular structure.

CAChe uses quantum mechanics to compute the force necessary to distort the molecule from its equilibrium geometry and predict the frequency of vibrational transitions. When you select a point on the vibrational spectrum, motion vectors for every atom appear in the workspace, as shown in the following example.



You can edit the spectra to adjust the peak width, wavelength, and area of a selected transition.

📖 NOTE UV-visible and vibrational spectra generation are not available in Personal CAChe and BioCAChe. However, it is possible to view the UV-visible and vibrational spectra in Personal CAChe and BioCAChe that have been created in other versions of CAChe.

Viewing infrared spectra

To view infrared spectra

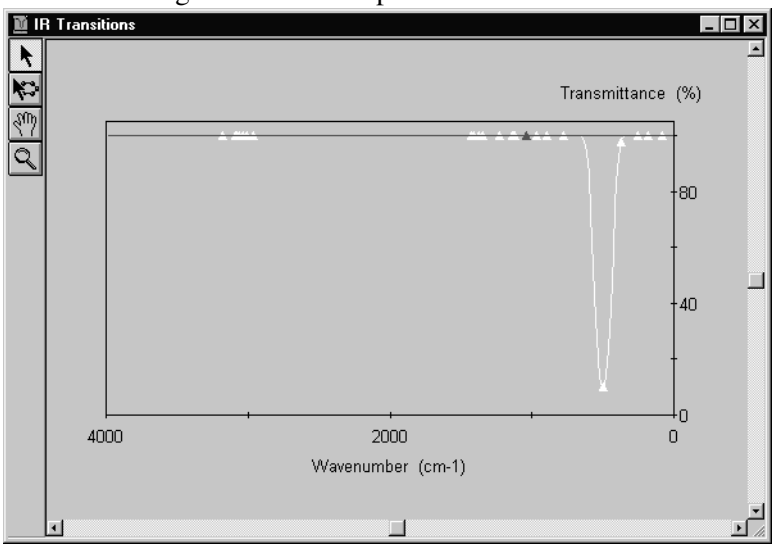
1. Open a chemical sample file for which you have infrared

(vibrational) spectra data.

2. Choose **Analyze | IR Transitions** to display the IR Transitions window.

   If you have more than one chemical sample file open with infrared spectra data, choose **Analyze | IR Transitions** for each file to display the associated spectrum in the IR Transitions window. Additional spectra are indicated by a legend, which is automatically displayed.

   The following shows an example of an IR Transitions window.



To view motion vectors

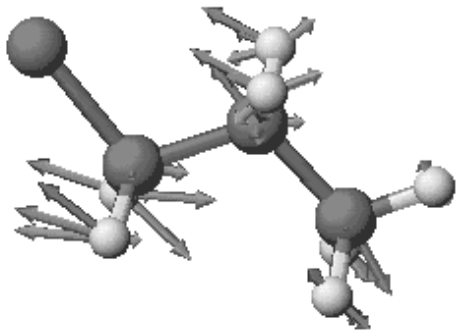
1. Using the Select tool, click a transition in the graph function, which is indicated by a triangle.

   The selected transition is highlighted in red to show that it is selected. Motion vectors indicating the direction of movement for each atom in motion appear in the workspace.

2. Hold down **Shift** and click repeatedly on triangles in the graph function to select several transitions.

   The selected transitions are highlighted in red and motion vectors belonging to all the selected transitions are displayed for each atom in the workspace.

The following example shows a display of motion vectors from several selected transitions.

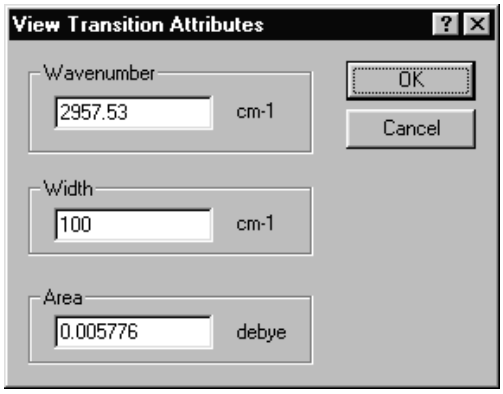


To edit transition properties

1. For a single transition, double-click the transition.

   For more than one transition, select the transitions for which you want to edit properties, then choose **View | Transition Attributes**.

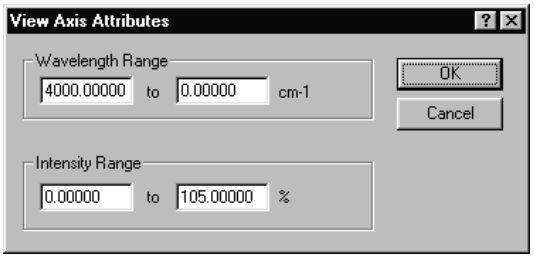
   The View Transition Attributes dialog box is displayed.



2. Click in the **Wavenumber**, **Width**, or **Area** text box to edit the peak width, wavelength, or area of the selected transitions.
3. Select **OK** to close the View Transition Attributes dialog box.

To change axis attributes

1. Double-click either spectral axis to display the View Axis Attributes dialog box.



2. Click in the **Wavelength Range** or **Intensity Range** text boxes to edit the range of each axis.
3. Select **OK** to close the View Axis Attributes dialog box.

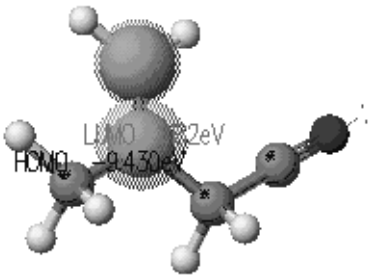
Investigating UV-visible spectra

📖 NOTE UV-visible spectra can be generated only if you have ZINDO.

CAChe enables you to view electronic spectra for a molecule, created by electron transition between molecular orbitals as electromagnetic radiation in the visible and ultraviolet (UV-visible) region is absorbed by the molecule.

Absorption bands observed in the UV-visible region are associated with changes of orbital occupations, so viewing electronic transitions helps identify excited states available for both kinetic and photochemical reactions. The relationship between structure and absorption aids the engineering of molecules with specific electronic absorption properties.

CAChe uses quantum mechanics to compute the energies of excited electronic states. When you select a particular spectral transition point on the electronic spectra, the molecule is displayed in the workspace with molecular orbital surfaces superimposed on it, as shown in the following example.



You can edit the spectra to adjust the peak width, wavelength, and area of a selected transition.

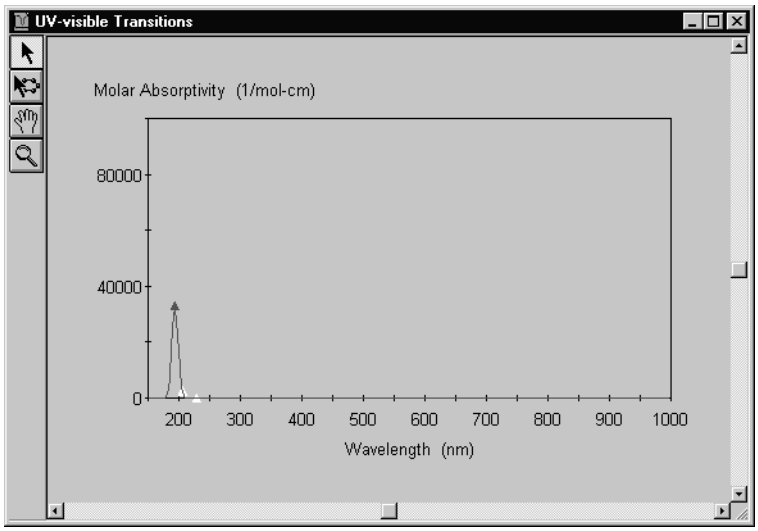
Viewing UV-visible spectra

To view UV-visible spectra

1. Open one or more chemical sample files for which you have UV-visible (electronic) spectra data.
2. Choose **Analyze | UV-visible Transitions** to display the UV-visible Transitions window.

   If you have more than one chemical sample file open with UV-visible spectra data, each individual spectrum is displayed in the UV-visible Transitions window, indicated by a legend which is automatically displayed.

   The following shows an example of a UV-visible Transitions window.



To view molecular orbital transitions

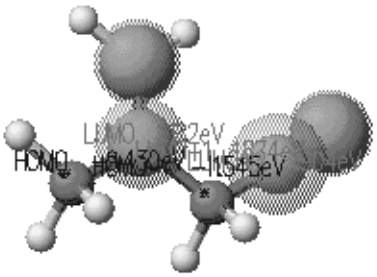
1. Using the Select tool, click a transition in the graph function, which is indicated by a triangle.

   The selected transition is highlighted in red to show that it is selected. Molecular orbital surfaces for the transition are displayed superimposed on the relevant atoms in the workspace. HOMO and LUMO energy values are also displayed.

2. Hold down **Shift** and click repeatedly on the graph function to select several transitions.

   The selected transitions are highlighted in red and molecular orbital surfaces belonging to all the selected transitions are displayed for each atom in the workspace.

   The following example shows a display of molecular orbital surfaces from several selected transitions.



To edit transition properties

1. For a single transition, double-click the transition.

   For more than one transition, select the transitions for which you want to edit properties, then choose **View | Transition Attributes**.

   The View Transition Attributes dialog box is displayed.

2. Click in the **Wavelength**, **Width**, or **Area** text box to edit the peak width, wavelength, or area of the selected transitions.
3. Select **OK** to close the View Transition Attributes dialog box.

To change axis attributes

1. Double-click either spectral axis to display the View Axis Attributes dialog box.
2. Click in the **Wavelength Range** or **Intensity Range** text boxes to edit the range of each axis.
3. Select **OK** to close the View Axis Attributes dialog box.

19 Investigating Biomolecules

Overview

This chapter explains how to use CAChe with biomolecules to:

- investigate peptide conformations
  - build a peptide using the Sequence View
  - explore conformations with CONFLEX
  - analyze conformations in the workspace
  - solvate the peptide with water molecules.
- build a GPCR 3D structure using homology modeling
  - read in the x-ray crystal structure of a homolog
  - use the Sequence View window to modify the seven transmembrane (TM) helical domains
  - use the Sequence View window to insert, delete and modify loops
  - solvate the GPCR model with a water shell
  - use mechanics and dynamics to refine the structure
  - validate the model

Contents

Investigating peptide conformations 19-3
Building a peptide 19-3
Generating peptide conformations 19-6
Analyzing peptide conformations 19-8
Including water 19-10
Creating a homology model of the MC4R 19-15
Viewing bovine rhodopsin 19-16
Building a model of MC4R 19-17
Docking Agouti-Related Protein into the MC4R 19-22

- dock a ligand into a protein.
  - locate the receptor
  - dock the ligand into the receptor using distance adjustments
  - refine the ligand-protein complex using mechanics and dynamics
  - model additional small molecule ligands using CONFLEX and property calculations with MOPAC
  - dock favorable candidates into ligand binding site by superposition on the original ligand

📖 NOTE The Sequence View is available only in CAChe WorkSystem Pro, BioCAChe and BioMedCAChe. Since this chapter uses the Sequence View, it is applicable only to WorkSystem Pro, BioCAChe or BioMedCAChe.

Investigating peptide conformations

CAChe enables you to build peptides from their sequence and search for their lowest energy conformations.

CAChe can use either molecular mechanics or quantum mechanics to compute the energies of the peptide structures. Most often, you will use molecular mechanics to determine the stable conformations of peptides because it is the fastest and most accurate method for organic structures.

Conformational analysis in the workspace allows you to locate the lowest energy conformations. Selected conformations can be refined further using quantum mechanics in MOPAC.

Building a peptide

To build a peptide efficiently from the Sequence View window first set the secondary structure type and then enter the sequence. After you have entered the sequence, set the turns, create any disulfide linkages and add terminal atoms.

To enter a peptide from its sequence

1. Open a new chemical sample file.
2. Choose **Analyze | Sequence** to display the Sequence View window. Refer to *"Working in the Sequence View window"*, p 9-18 for information on using the Sequence View.
3. Choose **Window | Tile** to show both the Sequence View window and the workspace simultaneously.



4. Choose the insert Residue tool.
5. From the style bar, set the secondary style to beta anti-parallel.



TIP Oxytocin is a small 9-residue cyclic peptide with the sequence Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-Gly-NH_2 (`C-Y-I-Q-N-C-P-L-G-NH2`) with a disulfide bond between the cystine residues. Oxytocin is a hormone secreted by the posterior pituitary that stimulates uterine contractions. Note that it has an unusual amino group on the C-terminal glycine.

6. Do one of the following
   - Type the 1-letter code for each residue.
   - From the style bar, choose the first residue. Then choose **Edit | Insert**.

   Continue typing or inserting until the sequence is entered.



   The residues appear connected in the workspace as the peptide is built.

TIP You can choose **Edit | Select All** and **View | Fit in Window** from the workspace to show the peptide as you build it.

Finally, you add the terminal groups so that the peptide ends with NH_3^+ and CO_2^- as expected in water solution.



To add terminal atoms

1. In the workspace, choose the Select tool.
2. Select the N-terminal atom.
3. Change the charge on the style bar to 1. The charge on N changes to +1.
4. Choose **Beautify | Valence**. The group is now NH_3^+.
5. Select the C-terminal atom.
6. Choose **Beautify | Valence**. The group should now be CH=O.

📖 NOTE If you are building oxytocin which has an unusual amino group on its C-terminal glycine, change the H to N and **Beautify | Valence**. Then skip to "**To create a turn**". Otherwise, for standard C-terminal CO_2^- groups follow the following steps.

7. Select the newly created H atom.
8. Using the style bar, change the atom type to O and the charge to -1. The H atom is replaced by O^-.
9. Select the CO_2^- group.
10. Choose **Beautify | Hybridization.**

    The hybridization changes to sp^2.
11. With only the CO_2^- group selected, choose **Beautify | Geometry**. Only the CO_2^- group changes.
12. Choose **File | Save** and save the peptide as a chemical sample.

    The peptide now terminates in NH_3^+ and CO_2^- terminal groups, the structure expected in aqeuous solution.

As you build a peptide you may need to enter turns, for example if the peptide is cyclic.



To create a turn

1. In the Sequence View window, choose the Select tool.
2. Select the two residues in the middle of the sequence where the turn is to be located. If you are building oxytocin, select residues 3 and 4 (Ile and Gln).
3. Choose **Edit | Make Turn | Type I**.
4. In the workspace, connect the sulfur atoms to make the cyclic peptide.
5. Choose **Beautify | Valence**.
6. Fix the ends to NH_3^+ and CO_2^-.

When the peptide is cyclic, you close the cycle by creating bonds in the workspace.

To create a cyclic peptide



1. In the workspace, choose the Select tool.
2. Select the two sulfur atoms for the disulfide bond.
3. Choose **Edit | Connect**.
4. With the two sulfur atoms selected, choose **Beautify | Valence**.
5. Choose **Beautify | Hybridization**.

A bond appears between the two sulfur atoms and the hydrogen atoms are removed.

You have finished building the peptide using standard templates for residues and standard bond angles and distances. At this point, your peptide may contain atoms that are too close together or bonds and angles that require refinement. You clean up the geometry by optimizing the structure with molecular mechanics.

To refine the peptide 3D structure

1. To optimize the structure, choose **Experiment | New**
2. Select these options in the experiment window:
   - **Property of | chemical sample**,
   - **Property | optimized geometry**, and
   - **Using | MM geometry (MM3)**.
3. Choose **Start**.

   The geometry is optimized using MM3.

Generating peptide conformations

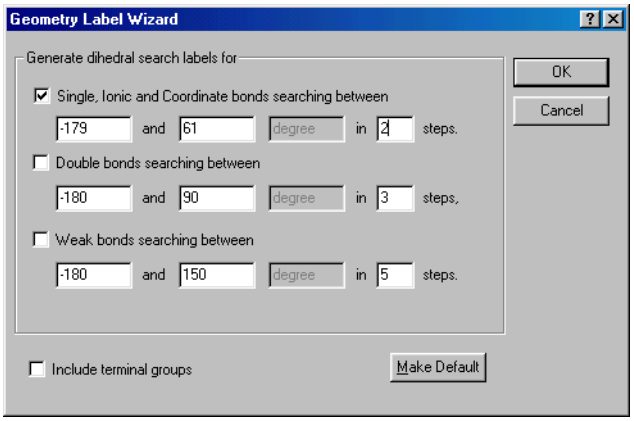
After you have built the peptide, you locate the lowest energy conformations.

To generate peptide conformations

1. Using the Select tool in the workspace, click on a rotatable C-C single bond joining the C atoms outside any rings in the peptide.
2. Press **Shift** and click repeatedly on each remaining rotatable C-C bond outside any rings to select several rotations.

   The selected bonds are highlighted.

3. Choose **Adjust | Geometry Label Wizard** and change the settings in the Geometry Label Wizard dialog so that rotations around single bonds are explored in two steps from -179 to 61 degrees

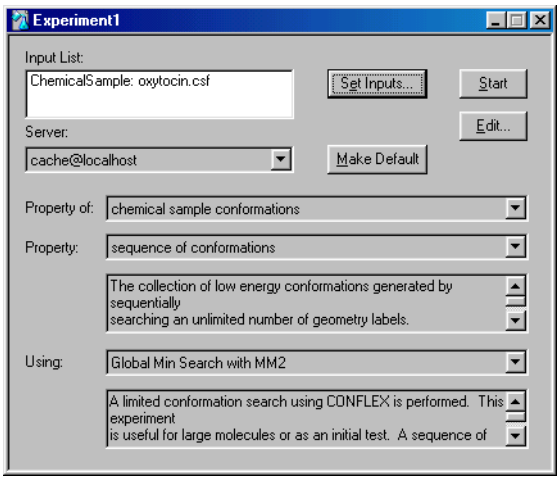


After making the changes so that the dialog appears as above, choose **OK**.

The peptide structure appears with dihedral labels displayed for each of the previously selected C-C bonds.

4. Choose **Experiment | New**. The Experiment dialog appears.
5. Choose
   - **Property of | chemical sample conformations**,
   - **Property | sequence of conformations**, and
   - **Using | Global Min Search with MM3**.

The Experiment dialog should look similar to this:



6. Choose **Start**.

   CONFLEX runs and automatically searches for low energy structures in rings and around the rotatable bonds that have search labels. For peptides, this is a lengthy process requiring many hours.

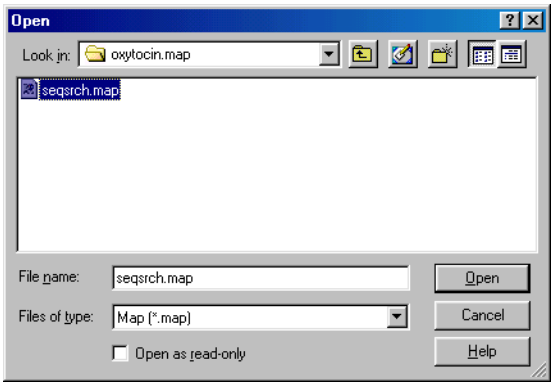
   When CONFLEX completes, it creates a sequence file in the .map directory and opens it automatically in the CAChe workspace if CAChe is running. You use the workspace to analyze the results from CONFLEX.

Analyzing peptide conformations

To analyze the peptide conformations

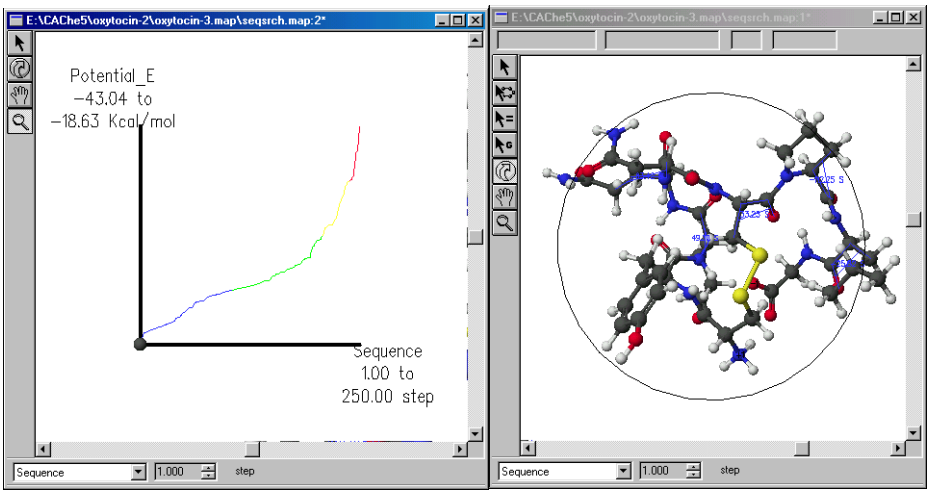
1. Choose **File | Open**, set the **Files of Type** to **Map (*.map)** and

navigate to the .map directory for your chemical sample.



2. Choose `seqsrch.map` and **Open**.

   Two windows appear side-by-side.



3. Click on the graph to move the ball to a new conformation. The 3D structure in the workspace changes to that of the newly chosen conformation.
4. Choose **File | Save As Chemical Sample** to save low energy conformations. As you save each conformation, you may find it useful later if you include the sequence number or the conformation number in the new file name.

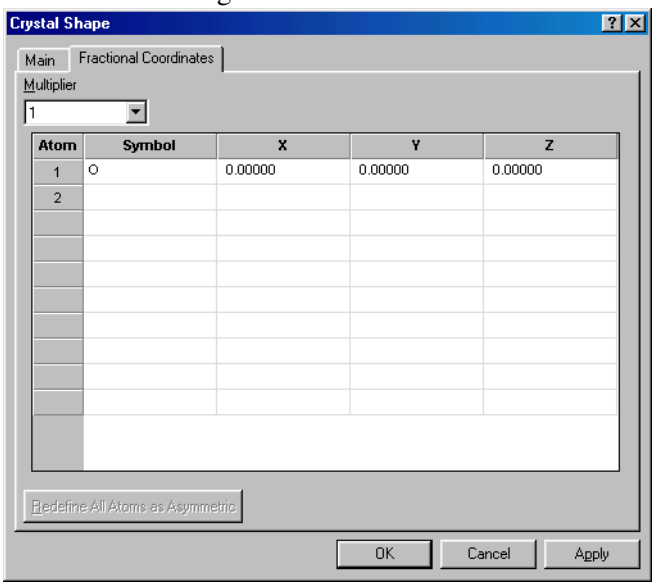
Including water

The conformations you found in the previous section are those for the isolated peptide. Without solvents, the ionic ends of the peptide will attract and the conformations with the NH_3^+ and CO_2^- groups near one another will be more stable. A polar solvent, like water, will stabilize extended structures. You can model the effect of solvation by adding water molecules to the peptide chemical sample.

To add water, it is useful to have a chemical sample containing water molecules.

To create a water droplet

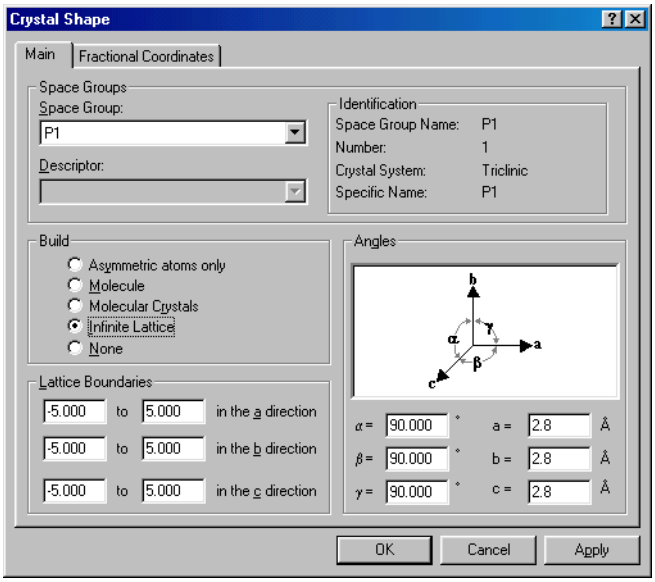
1. From the workspace menu, choose **File | New**. A new workspace opens.
2. Choose **Edit | Crystal Shape**. The Crystal Shape dialog opens.
3. Choose the **Fractional Coordinates** tab in the Crystal Shape dialog.
4. Enter 'O' for oxygen and set the fractional coordinates at 0., 0., 0. so that the dialog looks like this



After typing the last coordinate, press the Enter key to complete

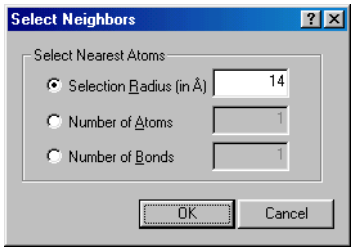
the row.

5. Choose the **Main** tab and set the space group to P1, the Lattice Boundaries to -5.0 to 5.0, and the a, b and c lengths to 2.8 angstroms. Finally, choose to build an **Infinite lattice**. The Crystal Shape dialog should look like this.



6. Choose **OK**. A 28 angstrom cube of 1326 oxygen atoms appears in the workspace.
7. Choose **Window | New Sample Properties Window**. The sample properties window appears.
8. Choose the **Atom** tab and select row 1. The oxygen atom at the center of the cube is selected.
9. In the workspace, choose **Edit | Select Neighbors**. The Select Neighbors dialog appears.
10. Choose to select nearest atoms by selection radius and set the

selection radius to 14 angstroms.



11. Choose **OK**. All atoms within a sphere of 14 angstroms from the central oxygen atom are selected.
12. Using the Select tool, invert the selection by holding down the shift key while clicking on empty space.

    All atoms outside the sphere are selected and those inside the sphere are unselected.
13. Choose **Edit | Delete** to remove the atoms outside the droplet.

    A sphere of 515 oxygen atoms remains. To retain the spherical shape during optimization, lock the outer shell of oxygen atoms.
14. In the Sample Properties Window, select atom 1 by clicking on the row number.
15. In the workspace, choose **Edit | Select Neighbors** and select neighbors within 11.5 angstroms of the selected oxygen atom.
16. Using the Select tool, invert the selection by holding down the shift key while clicking on empty space. The outer shell of oxygen atoms is selected.
17. Choose **Adjust | Lock** to lock the outer shell of oxygen atoms. The outer most atoms are locked.

    To display the locked state, choose **View | Atom Attributes** and check **Locked State** on the **Label** tab.
18. In the workspace, choose **Edit | Select All** and then choose **Beautify | Comprehensive** to add hydrogen atoms and set the hybridization.

    You now have a sphere of 515 water molecules (1545 atoms) all oriented in the same direction.
19. Choose **Beautify | H-Bonds**.

The hydrogen atoms are rotated so that the local hydrogen bonding is maximized. This is a partial optimization of the hydrogen bonding.

To further optimize the hydrogen bonding, you use Mechanics. Since you will be using this droplet to solvate molecules, it will be convenient to have the atoms grouped into a single group.

20. Choose **Edit | Select All** and then **Edit | Group Atoms**. Type a name for the group such as '11A water drop' and choose Group and then OK.

    All water molecules are now part of the same group named '11A water drop'.

21. To optimize the structure, choose **Experiment | New**, save the file and then choose

    - **Property of | chemical sample**,
    - **Property | optimized geometry**, and
    - **Using | MM geometry (MM3)**.

    Choose **Start**.

    The water droplet is optimized within the sphere of frozen oxygen atoms. You can use this droplet to add water molecules to your peptide.

To solvate the peptide

1. With both the water droplet and peptide open, choose **Edit | Copy** from the peptide workspace.
2. In the water droplet workspace, choose **Edit | Paste**.

   The peptide appears in the center of the water droplet. To reorient the peptide to a different position, choose **Edit | Move Selected** and rotate or drag to peptide to the position you prefer. Notice that some water molecules overlap the structure. You need to remove them.

3. To remove overlapping water molecules, use the Select Molecule tool to select the peptide.
4. Then choose **Edit | Select Neighbors** and **Select Nearest | Residues, waters, HETs** within 2 angstroms.

All waters, residues and HET groups within 2 angstroms of the selected peptide atoms are selected.

5. Using the Select Molecule tool, hold down the shift key while clicking on the peptide to deselect the peptide.

   The peptide dims and all water atoms near the peptide remain highlighted.

6. Choose **Edit | Delete**.

   Water molecules that overlap the peptide are deleted.

7. Choose **File | Save As** to save the model using a different name.

8. To complete the model, you optimize the solvated peptide. Choose **Experiment | New**. The Experiment dialog appears.

9. Choose

   - **Property of | chemical sample**,
   - **Property | optimized geometry**, and
   - **Using | MM Geometry (MM3)**.

10. Choose **Start**.

    A calculation that optimizes the geometry of the peptide within the water sphere of 11 angstrom radius using MM3 is performed.

Creating a homology model of the MC4R

During 2000, the first high resolution x-ray crystal structure of a G protein-coupled receptor (GPCR) - bovine rhodopsin - was determined[1]. GPCRs form a superfamily of homologous membrane-bound proteins important in cellular signaling and are targets for 60% of drugs in use or development.

Design of more active, selective and safe drugs that target GPCRs requires knowledge of other GPCR 3D structures. Unfortunately, because there are often relatively few molecules of a specific GPCR in each cell and because of the difficulty in growing the crystals, it is unlikely that the x-ray structure of other GPCRs will be determined.

GPCRs are membrane-bound proteins that are characterized by seven helical regions that traverse the lipid bilayer of the cell membrane. These transmembrane (TM) helices not only define the binding sites for ligands that can interact with the GPCR, such as hormones and neuropeptides, but also undergo conformational rearrangements that are an essential element of signal transduction and intercellular communication.

Since all GPCRs likely share a common ancestor, you can use the recent crystal structure of rhodopsin as the basis for building a high-quality model of other GPCRs using well-established homology modeling methods. In this GPCR have very similar “core” TM helical structures, even though there may be considerable variation in their amino acid sequences due to their different biological functions.On the other hand, since the mechanisms of GPCR activation are identical, a small number of amino acids in each TM helix are conserved and can be used to align the sequence with rhodopsin using algorithms such as CLUSTAL W.

Starting with an aligned sequence, you can use the Sequence View Window to modify the rhodopsin sequences to match the GPCR you want to model and then refine it with mechanics and dynamics following the protocols described in the following discussion.

1. Palczewski, K., Kumasaka, T., Hori, T., Behnke, C.A., Motoshima, H., Fox, B.A., Le Trong, I., Teller, D.C., Okada, T., Stenkamp, R.E., Yamamoto, M., and Miyano, M. Crystal structure of rhodopsin: A G protein-coupled receptor. *Science* **2000**, *289*, 739-745.

Viewing bovine rhodopsin

To view bovine rhodopsin

1. Open the bovine rhodopsin crystal structure `1F88.pdb` from the Protein Data Bank (http://www.rcsb.org/pdb).
2. Choose **Analyze| Sequence**.
3. In the Sequence View, choose the Select Molecule tool.

NOTE `1F88` contains two copies of bovine rhodopsin in the asymmetric unit. They are called chain A and chain B.

4. Select chain A. Copy it. Close the Sequence View Window. Note that you have selected only the sequence chain. The covalently modified sugars and retinal are in different chains and are not copied.
5. Open a new workspace. Paste the copied sequence into the new workspace. Note that there are two long bonds because some residues are not resolved in the crystal structure. They will be removed when the final homology model is constructed.
6. Close the `1F88` file.
7. Choose **File | Save** and save the structure as `bovine-rhodopsin.csf`.

   You will be warned about the large charge on the protein. Press **OK** and continue to save.

Building a model of MC4R

The melanocortin-4 receptor (MC4R), a GPCR which is expressed only in the brain, is involved in the control of human feeding behavior. The agouti-related protein (AGRP) functions as an antagonist of the MC4R. Over expression of AGRP in mice gives rise to increased food intake, making them obese. A 3D structure for the AGRP/MC4R complex could lead to structure-based design of drugs that treat eating disorders.

Here you build a model structure of MC4R from the structure of bovine rhodopsin and a sequence alignment of MC4R and bovine rhodopsin (OPSD_BOVIN).



To change the helices

1. Chose **File | Open** and open the `bovine-rhodopsin.csf` file

that you created in *"Viewing bovine rhodopsin"*, p 19-16.

2. Choose **File | Save As** and rename this file `MC4R.csf`.
3. Choose **Analyze | Sequence**. Refer to *"Working in the Sequence View window"*, p 9-18 for information on using the Sequence View.
4. Check **View | Residue Numbers | PDB**. A Sequence No. line appears in the Sequence View window containing the residue numbers from the PDB file.
5. Delete residues from M1 to A32. This deletes the first extra cellular segment of rhodopsin. This segment is not needed for the model of MC4R.



Choose the Select tool. Using the `CLUSTAL W (1.81) multiple sequence alignment` shown in the table above select each residue in bovine rhodopsin and use the Residue Type drop-down on the Style ribbon to change the rhodopsin



residue one at a time into the residues that are in MC4R.

The residue changes, but the backbone Phi and Psi angles remain unchanged from rhodopsin.

To change the loops

Insert loop residues present in MC4R but not in rhodopsin and delete loop residues present in rhodopsin but not in MC4R.

After all of the loops are constructed. Delete everything past the last long bond (R(~214)NCMV). Note that the first long bond has been fixed by adding residues in MC4R.

To refine the initial MC4R model

1. In the Sequence view, choose **View | Secondary Structure**. The line SS appears below the sequence. Letters in this line denote the secondary structure. H denotes a residue in a helix.
2. Select the residues in the first helix.

3. From the workspace, Choose **Edit | Group Atoms**. Type the **Group Name** `TM1` and choose **>>Group>>**. The group named `TM1` is added to the list of groups. Choose **OK**.
4. Switch back to the Sequence View and continue selecting helices and creating groups until all seven groups `TM1-TM7` are defined.
5. In the workspace, choose **Edit | Select Backbone** to select the backbone atoms.
6. Choose **Edit | Group Atoms**. Type the **Group Name** `backbone`. Choose **>>Group>>**.

   The group named `backbone` is added to the list of groups.
7. With the Group Atoms dialog still open, choose group `TM1` and then choose **S or G**. The selection (S) now contains the atoms in both the backbone and `TM1`. Continue the choosing TM groups and choosing **S or G** until the selection contains the backbone atoms and all seven transmembrane helices.
8. Type `locked backbone` into the Group Name field. choose **>>Group>>**. The group named `locked backbone` is added to the list of groups. Choose **OK**.
9. Choose **Adjust | Lock**. The backbone atoms in all the helices are locked.
10. Choose **Beautify | Valence** and then **Beautify | Hybridization**.
11. Choose **Experiment | New**. The Experiment dialog appears. Choose
    - **Property of | chemical sample**,
    - **Property | optimized geometry**, and
    - **Using | MM geometry (MM3)**

    Choose Edit and change the procedure to use **steepest descent**.for geometry optimization. Refer to *"Modifying a procedure"*, p 11-17.
    Choose the Choose **Start**. The energy is minimized using steepest descent.
12. When the experiment completes, start a new experiment **Using | MM geometry (MM3)**. Choose Edit and change the procedure to use **conjugate gradient**.for geometry optimization. Refer to

"Modifying a procedure", p 11-17.
The energy is minimized for 300 cycles with the locked atoms using the conjugate gradient method.

13. After the experiment completes, choose **File | Save As** and rename the file `MC4R-1.csf`.
14. Next, choose **Experiment | New**. Choose
    - **Property of | chemical sample conformations**,
    - **Property | dynamics trajectory**, and
    - **Using | MD simulation (MM3)**.

    Choose **Start** to do dynamics at 1000 K with the locked atoms for 50 ps.
15. After the experiment completes, choose **File | Save As Chemical Sample** and name the file `MC4R-2.csf`.
16. Choose **Experiment | New**. The Experiment dialog appears. Choose
    - **Property of | chemical sample**,
    - **Property | optimized geometry**, and
    - **Using | MM geometry (MM3)**.

    Choose Edit and change the procedure to use **steepest descent**.for geometry optimization. Refer to *"Modifying a procedure"*, p 11-17.
    Choose **Start**. The energy is minimized using conjugate gradient.
17. After the experiment completes, select one turn (4 residues) at each end of each helix and then choose **Adjust | Unlock**. Then start a dynamics experiment at 600K for 50 ps. Save the last structure from the trajectory and energy minimize.
18. Repeat the unlocking and the dynamics and optimization experiments at 600 Kelvin until all helices have been unlocked and optimized.
19. After the last experiment completes, choose **File | Save As** and name the file `MC4R-final.csf`.

    You have refined the homology model of the structure of MC4R.

Once the structure is created, you examine it to verify that the inter-helix interactions that participate in GPCR activation mechanisms are present[1]

1. Gether, U., and Kobilka, B.K. G protein-coupled receptors. II. Mechanism of agonist activation. *J. Biol. Chem.* **1998**, *273*, 17979-17982.
   Ballesteros, J., Kitanovic, S., Guarnieri, F., Davies, P., Fromme, B.J., Konvicka, K., Chi, L., Millar, R.P., Davidson, J.S., Weinstein, H., and Sealfon, S.C. Functional microdomains in G protein-coupled receptors. *J. Biol. Chem.* **1998**, *273*, 10445-10453.

Docking Agouti-Related Protein into the MC4R

Agouti-related protein (AGRP) functions as an antagonist of the MC4R and binds to the MC4R. Site-directed mutagenesis experiments suggest that a conserved Arg-Phe-Phe motif mediates key interactions of this protein ligand with the MC4R residues Gly-Cys-Val.

NOTE Docking requires some experimental information on which residues on the receptor bind to which residues on the ligand.

To view AGRP

1. Get AGRP (1HYK) from the Protein Data Bank: `1HYK.pdb`.
2. Open `1HYK.pdb` in the workspace.
3. Examine the structure and check that the structure is correct. Are double bonds where they are expected? Is the valence correct? Are charges correct?
4. Choose **File | Save** and name the file `AGRP.csf`.

To dock AGRP into MC4R

1. Open `MC4R-final.csf` and `AGRP.csf`.
2. Choose **Analyze | Sequence** from each workspace.
3. Select R24-F25-F26 in the AGRP sequence.
4. Select G92-C189-V186 in the MC4R sequence.
5. Choose **Edit | Superimpose Sequence**. Choose **Superimpose Target and Probe in New Window**. Choose **OK**.

   A new workspace opens with AGRP superimposed on top of the receptor in MC4R.
6. Choose **File | Save** and name the file `ACRP-MC4R.csf`.
7. Define distance labels between the
   - C-alpha atoms in R24 and G92
   - C-alpha atoms in F25 and C189
   - C-alpha atoms in F26 and V186

8. With the Select Molecule tool, select AGRP and choose **Edit | Move Selected**.
9. With the Rotate and the Drag tools, adjust the position of AGRP until the distance labels each are approximately 2 angstroms and atoms in AGRP are clear of the MC4R atoms.
10. Place a sphere of explicit water molecules about the extracellular regions as described in *"Including water"*, p 19-10.
11. Start an experiment to optimize the geometry using MM3.
12. Continue the refinement with dynamics experiments at 300 K for 200 ps.

You have created a 3D structural model for the complex between Agouti-Related Protein and MC4R.

Part four

Understanding CAChe

The following chapter explains the theories behind the CAChe computational applications and the way each application functions.

20 CAChe Computational Applications

Overview

This chapter explains in detail the theories and methods behind the following CAChe computational applications:

- Mechanics, which uses augmented MM2/MM3 parameters.
- Dynamics, which approximates the movement of atoms.
- MOPAC, which determines optimum geometry and electronic properties by solving the Schrödinger equation using MINDO/3, MNDO, MNDO-*d*, AM, PM3, or PM5 semi-empirical parameters. MOPAC also implements MOZYME, a linear scaling method for giant molecules.
- Tabulator, which converts CAChe computational results into three-dimensional surfaces.
- DGauss, which determines optimum geometry and the electronic properties of molecules by solving the Kohn-Sham equations in a self-consistent-field molecular orbital approximation.
- CONFLEX, which computes optimum geometry and potential energy maps.

Contents

Understanding Mechanics **20-2**
Understanding Dynamics **20-7**
Understanding MOPAC **20-11**
Understanding Tabulator **20-22**
Understanding CONFLEX **20-23**

Understanding Mechanics

This section provides reference information about the kinds of computations possible using molecular mechanics methods and specific information about the CAChe computational application Mechanics.

Mechanics concepts

The term molecular mechanics refers to methods of determining molecular geometries using equations from classical Newtonian physics. These methods describe the forces acting on atoms in molecules using empirically derived equations. Currently, several different molecular mechanics force fields are widely used. You may also hear molecular mechanics methods called force-field methods, or Westheimer methods.

Most molecular mechanics force fields include terms describing bond stretching, angle bending, torsional, and nonbonded interactions such as van der Waals and hydrogen bond interactions. The sum of all these terms constitutes the steric energy of the molecule. Steric energy is a type of potential energy, and here the terms steric energy and potential energy are used interchangeably.

Mechanics computes the net force acting on each atom in your molecule as the sum of the following energy terms:

- bond stretch
- bond angle
- dihedral angle
- improper torsion
- van der Waals
- electrostatics (MM2/MM3 dipoles or partial charges)
- hydrogen bond
- torsion stretch (MM3 only)
- bend-bend interactions (MM3 only).

The electrostatic term is calculated from dipole-dipole interactions for the standard non-augmented force fields. For the augmented force fields, the dipoles are decomposed in to atomic charges before evaluation. Partial charges can only be added to a structure if they already exist in the structure file.

The potential energy of the molecule varies as the nuclear positions of the atoms change, and can be thought of as a multidimensional potential energy surface. The potential energy surface has hills corresponding to strained high energy conformations, and valleys corresponding to low energy conformations.

The goal of molecular mechanics optimization is to adjust the positions of the atoms until finding an *optimum* molecular geometry. This optimum geometry corresponds to a minimum, or valley, in the potential energy surface. Molecular mechanics optimization techniques find an optimum geometry by systematically moving all atoms until the net force acting on each atom approaches zero.

The CAChe Mechanics application implements Allinger's standard MM2 force field and MM3 force fields.[1] CAChe significantly augments these force fields by providing rules that estimate the force field parameters for cases not addressed by the standard force fields. Augmentations enable minimization calculations for square planar, trigonal bipyramidal, and octahedral atoms.

The Mechanics computational application consists of the `MechanicsComputeEngine` and the `MechanicsManager`, both of which are located in the `Mechanics` folder in `cache/bin`.

Optimizing with Mechanics

Mechanics can be used in a variety of ways to help you find low energy conformations of your structure. When you use the **fastest procedure** or **MM geometry** procedures, Mechanics starts with the molecular structure in your chemical sample file. After calculating the structure's potential energy, Mechanics adjusts the atomic positions and calculates the potential energy of the new structure.

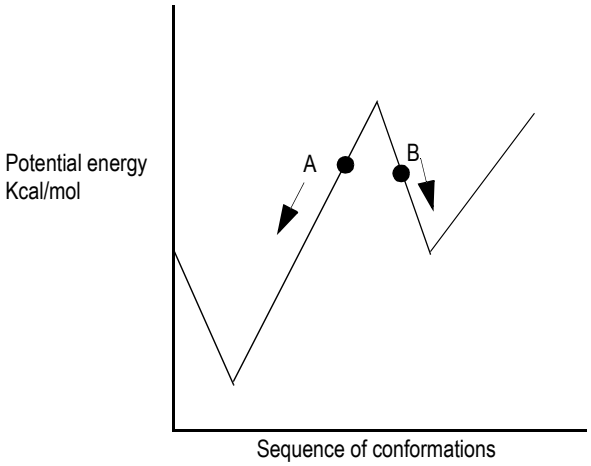
1. Allinger, N. L. and others, *J. Am. Chem. Soc.* **1977**, *99*, 8127; Allinger, N. L., Yuh, Y. H., Lii, J-H., *J. Am. Chem. Soc.*, **1989**, *111*, 8551-8566; Bowen, J. P., and Shim, J-Y., *J. Comp. Chem.*, **1998**, *19*, 1370-1386.

Mechanics then moves the atoms and calculates the energy until the energy reaches a minimum, and moving the atoms no longer decreases the energy. Mechanics continues optimizing until the energy change between iterations is within a specified limit, or until reaching the specified number of iterations. The direction and distance that atoms move between iterations depends on the slope of the potential energy surface.

Normally, optimizing is the next step after you create a molecule in the workspace and before proceeding to other computations. Most CAChe experimental procedures begin with optimizing a chemical sample.

The energy minimization procedure is an iterative process. Therefore, unless there is only one minimum in the potential energy surface, the final structure will depend on the starting geometry.

For example, the following graph shows how a starting structure from point A optimized to an energy minimum produces a different low-energy conformation than a starting structure from point B on an energy graph.



Generating energy maps with Mechanics

Mechanics uses search labels that you add to your molecule before beginning an experiment to generate an energy map.



Refer to Chapter 8, *"Investigating Molecular Geometry"*, for more information on search labels.

When you run the rigid map or optimized map experiment, a new assemblage file called `energy.map` is created and saved in an automatically generated folder named with the suffix `.map`.

Mechanics computes the energies of each conformation resulting from stepping the search labels through the defined range of values. The rigid map experiment keeps the structure rigid at the points where search label steps are defined. The optimized map experiment optimizes the conformation at each step. This computation restricts the relaxation of the molecular structure where search labels are defined (that is, the more search labels defined, the less relaxation that is possible during optimization).

Each combination of search labels and steps is computed when you generate an exhaustive map. That is, if you define two search labels, each with ten steps, your potential energy map will contain 121 conformations (11^2) because ten steps result in eleven conformations, and each one is tested in combination with all other possibilities. You can examine an energy map for up to eight search labels at one time, but it is impractical to employ this computation for more than three or four search labels in one molecule file, because of the time required to perform the calculations.

Generating a sequential search with Mechanics

Search labels you define in the workspace also serve as the basis for performing sequential searches with Mechanics.

When you compute the potential energy of multiple conformations of your molecule using the sequence of conformations experiment, the conformations defined by search labels are examined in sequence. A new assemblage file called `seqsrch.map` is created and saved in the automatically generated `.map` folder.

Mechanics begins this computation by performing a rigid energy search to find the best starting structure among those defined by the search label steps and ranges. To do so, it traverses each search label one step at a time. Beginning with the first search label, it determines the lowest energy position and holds it there while the lowest energy position of the second label is determined and held, and continues down the line of search labels. That first pass through all the search labels provides a starting structure for the sequential search.

In the **fastest procedure** and **MM one pass** procedures, the computation returns to the first search label, and for each step, optimizes the structure, while holding the internal coordinates defined for that step of that search label constant. The optimized structure that results from each step in each search label is saved in the `seqsrch.map` file. To examine, view the map file.

The `seqsrch.map` file is an assemblage file that contains a number of conformations equal to the number of steps (plus one) multiplied by the number of search labels. For example, if your structure contains eight search labels, each with five steps, the `seqsrch.map` file includes 6x8=48 conformations (five steps results in six conformations). As a result, the sequential search is a more economical computation than the optimized map, when your goal is to look for low energy structures.

If you choose the **MM multiple passes** option, you can reduce the bias caused by the sequential search traversing the structure once in a single direction. The multiple pass option examines the multiple minima that occurred in traversing the search labels. The multiple pass option takes more time, performs more computations, and captures more low energy structures.

In contrast to the optimized energy map, the sequential search focuses computational power and time on the low energy regions of the potential energy surface. When you perform a multiple pass sequential search, you are likely to obtain the same low-energy conformers that are found by an optimized map. However, these conformations will be closer to the true minima, because this computation allows the relaxation of the entire structure apart from the searched label.

The sequential search is also a more economical computation, so you can compute more search labels in less time than the exhaustive map.

Understanding Dynamics

This section provides reference information about the kinds of computations possible using dynamics methods and specific information about the CAChe computational application Dynamics.

Dynamics concepts

Dynamics methods approximate the movements of atoms. The potential energy of a molecular system is governed by the empirical force field. The CAChe computational application Dynamics uses the same force fields as the Mechanics application. The kinetic energy of a molecular system is derived from the atomic velocities, which in turn are chosen to reflect the temperature of the simulation. By executing Dynamics simulations, you can observe the molecular systems that you are studying in motion.

While Mechanics methods can produce low-energy conformations for molecular systems, they offer no information about the motions of the atoms. A molecular dynamics trajectory approximates the real motions in a molecular system by using the same force field equations that describe the potential energy of a molecule in terms of molecular geometries to evaluate the forces on each atom.

By integrating Newton's equation of motion, atomic velocities can be obtained from the forces on each atom. For any given temperature, an initial set of velocities can be selected from the Maxwell-Boltzmann distribution and a trajectory through time can be generated for any molecular system.

The CAChe Dynamics program uses the same force fields as the CAChe Mechanics program, and it utilizes the Verlet algorithm to update the velocities. The Verlet algorithm is a second order numerical integration of Newton's equation of motion. This dynamics simulation conserves the total (potential plus kinetic) energy, and the volume of the entire system. This type of simulation is also known as a microcanonical ensemble at temperature T.

Dynamics is intended to provide a window into the types of internal motion molecules undergo. While it attempts to duplicate real

molecular motions, there are some practical considerations that you should be aware of.

Temperature

For simple particles, the temperature of a system is related to the average kinetic energy (as translational energy) for the molecules present $\overline{KE} = \frac{3}{2}kT$. For polyatomic molecules, additional energy is found as rotational motion of the molecule and vibrational motion of the atoms, $\overline{KE} = \overline{KE}_t + \overline{KE}_r + \overline{KE}_v$.

For anything but a linear molecule, $\overline{KE} = \frac{3}{2}kT + \frac{3}{2}kT + \frac{1}{2}NkT$, where N is the number of degrees of vibrational freedom. For nonlinear molecules, N = 3 x number of atoms - 6. Thus the total kinetic energy of a large molecule is larger than that of a small molecule at the same temperature.

In the CAChe Dynamics simulation, the molecule remains centered with no rotation, that is, with no net translational or rotational momenta. The motions you observe are only vibrational (stretching, bending, and internal rotation) motions of the atoms where their average velocities are determined from the relationships:

$$\overline{KE} = \sum_{i}^{i=N} \frac{1}{2} m_i v_i^2 = NkT \text{ and } \bar{v} = \sqrt{\frac{kT}{m}}$$

The velocity of each atom is determined using random selection from a Gaussian distribution of velocities around its average velocity. The amplitude of motion varies with the square root of the temperature. This relationship is true for molecules of all sizes although the collective motions possible in large molecules may create an illusion of more vigorous motion.

Relating temperatures and the motions of molecules in dynamics to our theoretical understanding requires some care. In CAChe Dynamics simulations, the molecule is alone in a vacuum. Thus, it never collides with another molecule, and, as a result, never changes energy or the pattern of motion.

Once the initial random velocities have been selected, the fate of the simulation is established. In simple molecules, this may be easily noticeable as a somewhat limited range of motions. For larger

molecules, the larger number of degrees of freedom will lead to more complex motions but will still not cover every configuration.

One application of Dynamics simulations is to search for nearby energy conformations. We may know that in real molecules a particular rotational barrier is easily crossed at a given temperature. However, the probability of catching a molecule in the process of crossing the barrier may not be very high. CAChe Dynamics simulations should behave similarly, but as in real life, will require some repeated simulations.

Normally, you should start with a minimized structure for a simulation. Sometimes the random velocities given to the individual atoms partially cancel each other and do not lead to the rotational motion expected. This is especially a problem with symmetrical groups like methyl, and in small molecules.

A simple approach to obtaining greater rotational motion is to start the simulation with the group rotated somewhat away from the minimum conformation. This does have the effect of increasing the average temperature slightly but if the rest of the molecule is minimized, no problems should arise. Use this approach with caution, and only with small portions of the molecule.

Generating a Dynamics trajectory

CAChe Dynamics generates a trajectory according to the settings that you specify. A trajectory is a collection of structures arranged sequentially in time. Each structure has a potential and a kinetic energy associated with it, as well as a temperature. You can examine the energies and the related structures simultaneously in two side-by-side windows by opening the map file dynamics.map, which is created when you perform an experiment in Dynamics. Generating trajectories can give you information about:

- the various conformations that occur as a result of normal molecular motion
- the structure-energy relationships of the molecule

- regions of the conformational space occupied by the system when applying a high temperature, and therefore a large amount of kinetic energy, to give the molecule enough energy to escape a local energy minimum.

Understanding MOPAC

MOPAC, the Molecular Orbital Package, developed by James J. P. Stewart, provides a choice of methods for computing electronic properties of molecules. CAChe provides access to MOPAC methods through a Windows environment.

This section provides reference information about the kinds of computations possible using MOPAC theory and specific information about the CAChe computational application MOPAC.

Use MOPAC to compute:

- bond orders
- dipole moments
- dynamics maps
- ionization potentials
- molecular orbital energies
- optimum geometry
- partial charges
- potential energy maps
- intersystem crossings
- reaction pathways
- transition states
- vibrational frequencies and spectra
- structure and properties in solution

MOPAC concepts

The CAChe MOPAC (Molecular Orbital Package) application determines both an optimum geometry and the electronic properties of molecules by solving the Schrödinger equation using the semi-empirical Hamiltonians AM1, PM3 and PM5, developed by M. J. S. Dewar and J. J. P. Stewart respectively. CAChe also supports the

older parameter sets MNDO and MINDO/3 and the newer parameter set MNDO-*d*. In addition, CAChe extends AM1 to AM1/*d*.

The molecular orbitals, heat of formation, and molecular geometry derivatives obtained are used to calculate vibrational spectra, molecular geometries, force constants, and other properties of molecules, radicals, and ions. These quantities are used to calculate reaction trajectories and to investigate chemical reactions by locating transition states.

MOPAC can calculate the geometry, energetics and reaction profiles of molecules in their excited states. It can include solvent effects in these calculations. Excited state calculations are important in simulation of photochemical processes.

MOPAC calculates heats of formation, rather than the energy required to separate the molecule into isolated nuclei and electrons as in quantum-chemical methods such as Extended Hückel Theory and ZINDO. In this section, energy and heat of formation are used interchangeably.

Although MOPAC uses many concepts from quantum theory, thermodynamics, and advanced mathematics, a detailed understanding of these areas is not necessary. MOPAC was written and designed with non-theoretical chemists in mind.

In CAChe, one version of the MOPAC application is available (`MOPAC2KComputeEngine`) MOPAC is also available on CAChe GroupServers.

How MOPAC differs from Mechanics

MOPAC is a quantum-mechanical method. Molecular Mechanics is a classical description using equations from Newtonian physics based on the atom hybridizations and bond types you draw when you build a molecule. Quantum mechanical methods use the Schrödinger equation to determine bond strengths, atomic hybridizations, partial charges, and orbitals from the positions of the atoms and the net charge. Because quantum mechanical methods describe bonds, they can describe chemical reactions in which bonds are formed and broken.

MOPAC calculates the heat of formation, whereas the energy calculated in molecular mechanics is the steric energy.

Both MOPAC and Mechanics recognize locked geometry labels, and atoms with locked workspace coordinates, that you define in your chemical sample file.

Both MOPAC and Mechanics can use search labels to create energy maps. You can use several search labels in Mechanics, but MOPAC is limited to one or two search labels. If you use one search label, the result is a reaction coordinate search. If you use two search labels, the result is a grid search. If you define more than two search labels, MOPAC ignores the additional ones.

MOPAC maps are preferred for mapping bond breaking and bond formation. Maps generated by Mechanics for bond breaking and bond formation are meaningless.

You can generate four different kinds of potential energy maps when using MOPAC. If you use one search label, you can choose to compute the heat of formation at each geometry defined by the search label, without optimizing other internal coordinates, or you can choose to optimize the internal coordinates for each geometry. Similarly, if you use two search labels, you can compute the heat of formation at each geometry defined by the search labels, with or without optimizing other internal coordinates.

MOPAC uses search labels in the same way as Mechanics. When you generate energy maps using MOPAC, it is best for the geometry of the molecule to be at an extreme in the range of values used for the steps. A map file (`*.map`) is produced, just as in Mechanics.

Mechanics puts the molecule strain energy into map files, whereas MOPAC adds heat of formation when you execute grid searches and reaction coordinate searches.

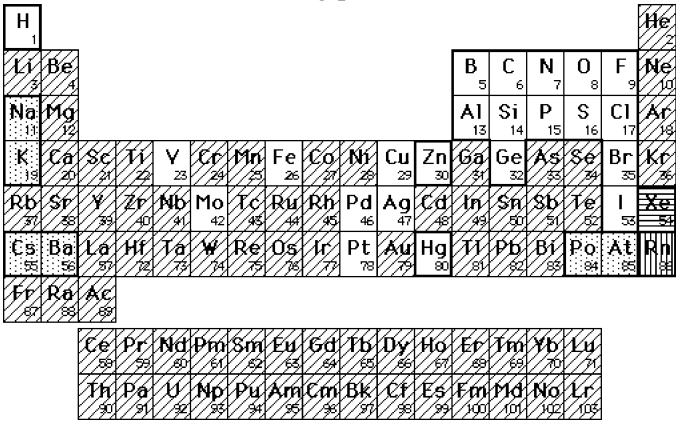
Mechanics calculations are simpler than quantum mechanical calculations. Consequently, Mechanics is much faster than MOPAC. The time required for molecular mechanics increases as the square of the number of atoms, whereas the time required for a MOPAC calculation increases as the cube of the number of atoms unless the linear scaling method for large molecules (MOZYME) is used.

Limitations of MOPAC

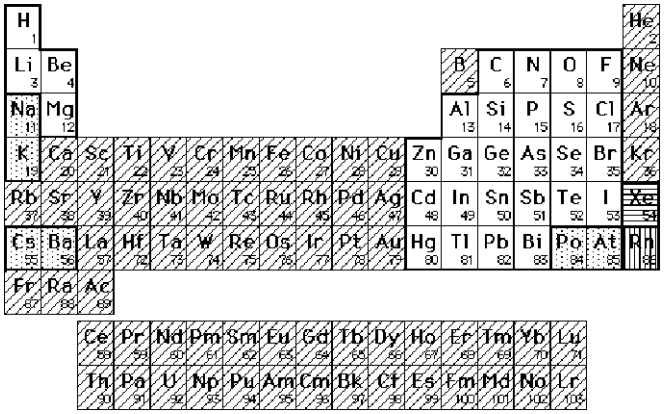
MOPAC is a valence-electron-only program and cannot calculate properties that depend upon changes in the inner-shell electrons. The valence-only nature of any semi-empirical method can manifest itself in unexpected ways. For example, electron isodensity surfaces can have an unusual appearance. Because valence-only theories do not treat inner-shell electrons, the calculated electron density near the nuclei is very small. Electron isodensity surfaces calculated at high density values may show no density around some atoms. The absence of density around some atoms emphasizes the valence-only approximation used in semi-empirical methods.

Elements parameterized in MOPAC

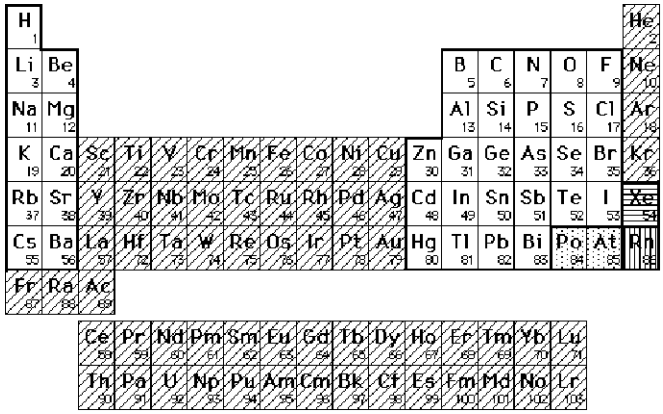
MOPAC contains AM1/*d* parameters for the elements indicated (not crossed off) in the following periodic table:



MOPAC contains PM3 parameters for the elements indicated (not crossed off) in the following periodic table:



MOPAC contains PM5 parameters for the elements indicated (not crossed off) in the following periodic table:



For the AM1/*d*, PM3 and PM5 Hamiltonians, Rn serves as a capped bond (Cb) element. Cs, Ba, Po and At serve as +, ++, --, and - sparkles, respectively. Xe serves as a dummy atom for all the Hamiltonians. When MOPAC encounters one of these elements in your molecule, it substitutes the appropriate symbol. Also, when CAChe processes the results of your MOPAC calculation, it replaces the MOPAC symbolic atom with the original element in your molecule.

A capped bond (Cb) behaves like a monovalent atom, with the exception that it can alter its electronegativity to achieve exactly zero

charge in whatever chemical environment it finds itself. It can thus mimic an exactly covalent bond with any atom. For example, on bonding to a hydrogen, it is similar to a hydrogen, but if it is bonded to a fluorine atom, it behaves like a very electronegative atom. If several capped bond atoms are used, they behave independently. Capped bonds can be used to mimic additional atoms that have been truncated from a crystal structure.

📖 NOTE It is essential that capped bond atoms be placed at a distance of 1.7 Å from the atom they are bonded to and that this bond distance be locked so that spuriously large gradients are not calculated. Electronic property surfaces cannot be tabulated for molecules that contain capped bond atoms.

Sparkles behave like 100% ionizable elements. For example, a ++ sparkle appears much like a barium atom. Sparkles represent the neutral atom. For example, if you wanted to represent the alkaline metal salt of formic acid, the formula would be HCOO+ (HCOOCs in the workspace).

The positive sparkle will donate its electron to the formate ion, and the molecule will be neutral. Na and K also act as + sparkles, but they appear as Na and K in the input file. Sparkles have no orbitals, no heat of atomization, and no ionization potentials. They have ionic radii of 0.7 Å, so that two sparkles of opposite sign will form an ion pair with a separation of 1.4 Å. The ++, +, -, and -- sparkles are assigned very large masses (10^8 a.u.) so that they behave as fixed points in vibrational spectrum calculations.

📖 NOTE Electronic property surfaces cannot be tabulated for molecules that contain sparkles atoms.

Optimizing with MOPAC

Stationary geometries are those for which the energy does not change when the atoms are displaced by infinitesimal amounts. This means that the net force on each atom is zero.

Minimum-energy geometries are stationary geometries for which the energy increases when the atoms are displaced in any direction. This means that the force constants of a molecule at a minimum-energy geometry are all positive. Because the force constants are all positive, the vibrational frequencies are all real.

The expression optimization refers to finding a minimum-energy geometry of the molecule. The minimum-energy geometry found is usually close to the starting geometry.

Other molecular geometries besides minimum-energy geometries are stationary. These include saddle points, inflection points, and hilltops. Of these, the saddle point is of greatest interest to chemists. Saddle points are also called transition states. See the next section for more information about saddle points.

MOPAC can use search labels to generate maps for optimized geometry. A reaction coordinate search uses one search label, and a grid search uses two. The first label listed in the molecule file will be used. All optimize map calculations are done in internal coordinates, MOPAC will override any attempt to use cartesian coordinates.

Transition states in MOPAC

Saddle points are stationary geometries for which the energy increases when atoms are displaced in all directions except one. This means that only one of the force constants of a molecule at a transition state geometry is negative, and all the rest are positive or zero. The vibrational frequency of the normal mode with the negative force constant is negative. On an energy map, a saddle point is at the top of the pass that connects two minimum-energy geometries with each other. Chemically, this geometry is a transition state.

The reaction coordinate is the direction of greatest energy decrease from the saddle point. The reaction pathway is the minimum-energy path from reactants to transition state to products.

MOPAC has a method designed for locating transition states, called a SADDLE calculation. Both the reactant and product molecules are specified, and MOPAC attempts to locate a stationary point that corresponds to the transition state for the reaction.

The geometry generated from a saddle calculation can be some distance away from the transition state. However, refining this structure through a minimize gradient calculation, usually leads to a structure closer to the transition state.

Another method for locating transition states is to perform a grid search calculation in which the two internal coordinates varied are the principal deformations that occur in the course of the reaction. The map that is produced may contain a pass on the energy surface that is a saddle point. The molecular geometry at this point can be used as an estimate of the transition state geometry.

The geometry of the transition state is refined with an optimization method that can minimize the energy gradient without searching for a minimum-energy geometry. Once the stationary geometry has been found, the transition state is characterized by calculating the vibrational frequencies for the molecule and verifying that there is one (and only one) frequency that corresponds to a negative force constant. These frequencies are negative (strictly speaking, they are imaginary, but they are reported as negative numbers as a matter of convenience).

Vibrational frequencies reported in the MOPAC output file contain six (or five, for linear molecules) vibrational modes, which correspond to translation and rotation of the molecule as a whole. These vibrations have frequencies that are close to zero if the molecule is at a stationary point. However, they will not be identically zero, because of the numerical approximations made in determining the stationary-point geometry and in calculating the force matrix.

Dynamics calculations in MOPAC

Two types of dynamics calculations are possible with MOPAC. The results are saved as an assemblage file (`drc1.map`, `drc-1.map`, `irc1.map`, `irc-1.map`).

With an Intrinsic Reaction Coordinate (IRC), you calculate the path in which all kinetic energy is lost at every step. As the potential energy changes, the kinetic energy generated is annihilated so that the potential and total energies are the same. An IRC follows the reaction path from the transition-state geometry to either the reactants, or products of the reaction. It simulates one effect of a reaction in a solution, in which all excess kinetic energy would be lost at every step of the trajectory. Other effects, such as the solvent dielectric, are not simulated by the IRC.

The IRC is intended to be used with a transition-state geometry as the starting point. You choose a vibrational mode for the initial motion. This vibration is usually the reaction coordinate. You also choose whether the initial geometry is displaced in the positive or negative direction along this vibrational mode.

With a Dynamic Reaction Coordinate (DRC), you calculate the dynamics trajectory that conserves energy. As potential energy is lost, the kinetic energy increases, so that the total energy is constant. DRC calculations may be run from any geometry. An internal coordinate can be specified for the initial displacement.

If the initial geometry is a transition state, an initial displacement along a particular vibrational mode is necessary. You choose the initial displacement by specifying a vibrational mode and a positive or negative direction for the initial motion. A DRC with no damping simulates the motion of the atoms of the single molecule in the gas phase, where none of the kinetic energy gained from losing potential energy would be lost, and would thus be converted into kinetic energy.

For DRC calculations, you may specify that only geometry information is output and included in the map file when atom coordinates, the heat of formation, or time has changed by a certain amount. This is useful when you want to run the trajectory for a long time, but do not want to generate very large output files.

Modeling solvent effects with COSMO

MOPAC contains a method for modeling the effect of highly polar solvents. COSMO (Conductor-like Screening Model), developed by Klamt and Schüürmann, approximates the dielectric screening

energy of a solvent by the method of image charges. It assumes that the medium is a conductor. For water, this is a very good approximation. The method is generalized by constructing a conducting polygonal surface based on the van der Waal's atom radii and an effective solvent radius.

A good example of the method is modeling the solvent effect of water on the geometry of alanine. In the gas phase, MOPAC predicts that neutral alanine (H2N-CH2-CH2-COOH) is more stable than the zwitterionic form (+H3N-CH2-CH2-COO-). When COSMO is used to model the solvent effects, the zwitterion is correctly predicted to be more stable.

Because COSMO includes solvent effects for energy gradients as well as energy, it is applicable to all types of MOPAC calculations. However, because COSMO requires a considerable amount of computation, it should not be used unless solvent effects are important.

Because of extra memory usage, calculations that use COSMO cannot handle as many atoms as those that do not use it. The practical limit depends upon computer speed and memory but for most computers the practical limit is approximately 200 atoms.

Large molecules

MOPAC contains a patented method called MOZYME that alters the way in which the electronic structure is calculated. As a result, calculations on large chemical systems require on a small fraction of the memory needed for a conventional calculation and run very much faster.

MOZYME can be used for simple geometric calculations, such as geometry optimization and transition state location, and for the calculation of polarizability.

There are limitations when this option is used.

- Only closed shell RHF calculations are allowed. Thus large molecule calculations are limited to chemical samples in their ground state. Radicals electronic excited states cannot be run.
- The results are not so precise. For calculations that need high precision MOZYME should not be used.

- Although the SCF uses only a small fraction of the memory needed by an equivalent MOPAC calculation, there is no way to reduce the memory needed for geometry optimization. The EF method uses a large amount of memory, and should therefore not be used in optimizing the geometry of very large systems. A better choice is LBFGS, although it, too, uses a lot of memory. When the geometry of a large system is optimized, the run should be broken into a series of short calculations, of 50-200 cycles. This is necessary because the geometry might change considerably during the optimization, and atoms that were not interacting at the start of the calculation might interact strongly at the end of the run. By stopping and restarting the optimization, any new interactions are taken into account. Failure to break up an optimization in this way can lead to a ruined calculation.

Understanding Tabulator

The Tabulator application converts the results of CAChe computational methods into three-dimensional surfaces and properties that you can view from the chemical sample file. This operation is needed to visualize electron density, molecular orbital, electrostatic potential, superdelocalizability, and amplitudes of UV-visible absorption surfaces. The Tabulator uses the molecule file as input, and produces new output isosurface files.

Tabulator concepts

To convert the results of some CAChe computations into three-dimensional graphics data, the Tabulator computes the value of wavefunctions at all points in a three-dimensional grid. To derive an isosurface, the Tabulator connects points of the same value throughout the grid.

The Tabulator uses as input the wavefunction data generated by the computational applications. Recall that ExtHückel, MOPAC, ZINDO and DGauss compute wavefunction data for all molecular orbitals, but you can save a subset of the data in your molecule file. You can tabulate data and visualize properties for any subset of the data that you saved in your chemical sample file.

The Tabulator carefully orders the molecular orbitals according to increasing energy. This may not be consistent with the numbering order in ExtHückel, MOPAC, ZINDO and DGauss. Therefore, molecular orbital numbers reported by the Tabulator may not exactly correspond with the molecular orbital numbers reported by the other applications, especially MOPAC and ZINDO.

Tabulator computes coordinates for an electronic property of your molecule once the computational applications have finished calculating the property. Tabulator creates separate isosurface files for each property you tabulate. You do not open the isosurface file to view the electronic property. Open the chemical sample file and choose the relevant menu options to view the data stored in isosurface files.

Understanding CONFLEX

CONFLEX generates low-energy conformers of a molecule of any shape. CONFLEX incorporates several unique strategies to complete a conformational space search:

- down-stream/reservoir-filling
- a variable search limit
- three modes of perturbation (unique corner flap, edge flip, and stepwise rotation)
- pre-check.

This section provides reference information about the kinds of computations possible using CONFLEX theory and specific information about the CAChe computational application CONFLEX.

Use CONFLEX to compute:

- optimum geometry
- conformations
- potential energy maps.

CONFLEX concepts

For convenience, the structures being processed are given different names, as follows:

- input structure is the input at the beginning of a search
- initial structure is called in from the conformer storage at the beginning of each perturbation cycle
- starting (trial) structure is the perturbed structure before geometry-optimization
- optimized structure is the structure after geometry-optimization
- stored structure is the optimized structure that survived the redundancy test, and it is saved in the conformer storage.

The algorithms for searching conformational space or a torsional hypersurface involve repeated sampling from the vast conformational space. The process, which is illustrated on the following page (a curved arrow indicates a looping subprocess), has the following steps:

(1) generation of an appropriate starting structure

(2) geometry-optimization of the starting structure

(3) comparison of the optimized structure with the stored conformers.

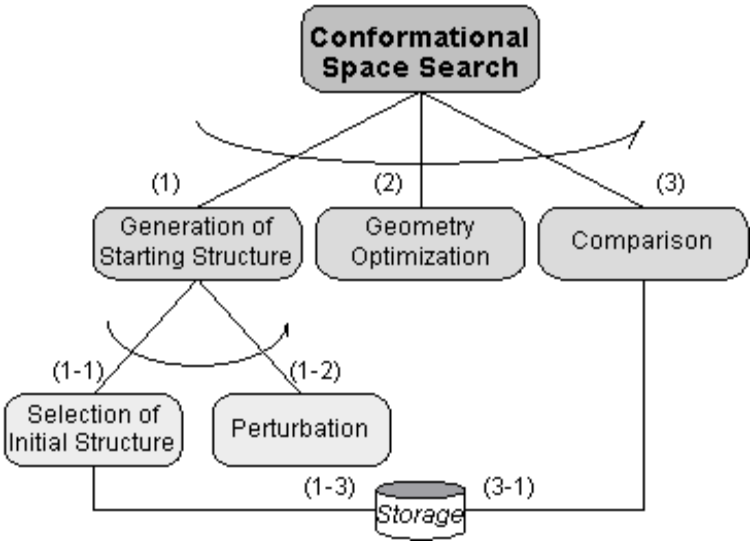
Finally, a structure passing all comparisons is added to the list of stored conformers.

In the advanced conformational-space search-algorithms, the first step consists of two subprocesses:

(1-1) selection of an initial structure from among the stored conformers

(1-2) assignment of appropriate structural perturbation to the initial structure to produce the coordinates of a starting structure.

Whereas the overall scheme is similar to most of the known conformation-generators, new strategies have been implemented for each step. In the following sections, these strategies are described.



The structures used in each process are:

Input and Output Structures

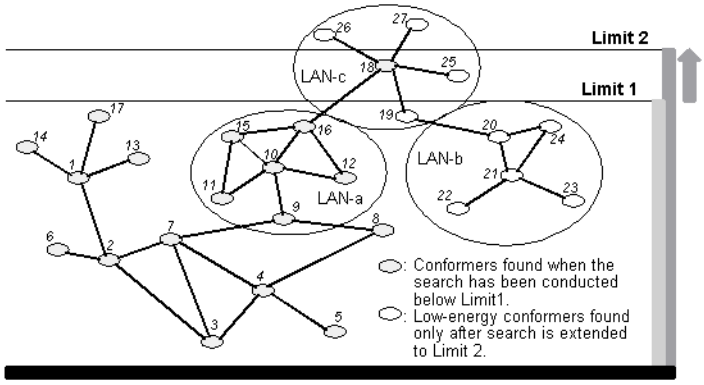
Process	Input	Output
(1)	None[a]	Starting
(1-1)	None or Stored	Initial
(1-2)	Initial	Starting
(1-3)	None	Stored
(2)	Starting	Optimized
(3)	Optimized	None/Optimized
(3-1)	Optimized	Stored

[a] At the beginning, no input structure exists in the conformation storage.

Generation of starting structure

The lowest-energy structure of the unused, stored conformers is chosen as the initial structure (a structure is considered to be unused if it has never been perturbed to generate a starting structure). This strategy is important to search through the region in the conformational space, in the most efficient way towards a lower

energy area. This is similar to a stream filling an empty reservoir by finding the the lowest point.



The strategy is illustrated schematically here for a conformational space search by the reservoir-filling algorithm.

- The initial structures are sampled in the numbered order given to the conformers (ellipses). A pair of conformers connected by a line comprise an initial structure and a conformer generated from that initial structure through perturbation and geometry-optimization.
- When the search limit is set to the level of Limit 1, the search is complete after the initial structures 1 through 17 have been processed.
- Then the search limit is increased to Limit 2, and conformers 18 through 25 are subjected to initial structures.

Variable search limit

When the global minimum or the instant global minimum in a local area is reached, the search moves towards a higher-energy area, and sometime local dips are overlooked in the process. The gradual expansion can be utilized to guarantee the thoroughness of the low-energy search.

The search limit is first decided, for example 5 kcal/mol from the global energy minimum, and all the conformers within this first

window (Limit 1) are used as the initial structures. During this search, all the conformers are saved, even those with energies higher than Limit 1.

The limit is increased to Limit 2 and all the conformers in the new window (between Limit 1 and 2) are subjected to initial structures in order of increasing energy. If local networks of conformers (LAN-a and LAN-b) are not connected within the first window, LAN-b is searched after LAN-c in the second window. A window width of 7 to 10 kcal/mol from the global minimum is generally sufficient to achieve an exhaustive search of the first, chemically meaningful window. Therefore, the variable limitation technique is a useful strategy for keeping the search region under control in the universal search.

Local perturbation

If the perturbation cannot move the starting structure from the territory to which it initially belonged, subsequent geometry-optimization will return it to the same structure. The territories of similar conformers may be located in close vicinity in the conformational space, constituting a local network of local territories, and less similar conformers may be considered to belong to different localities. Therefore, the method of perturbing an initial structure to produce a candidate new conformer is also responsible for the efficiency of search.

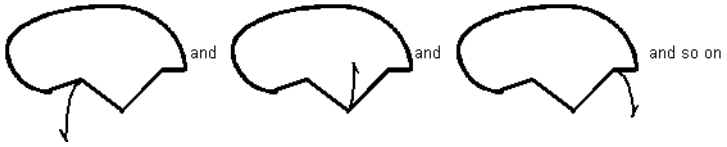
To ensure exhaustive generation of all possible starting structures, local perturbation is applied to every flexible part in the initial structure. The following three modes of perturbation are designed to mimic the elementary process in the thermal movements of a molecule undergoing conformational change: *corner flap* and *edge flip* for endocyclic parts, and *stepwise rotation* for acyclic parts.

Corner flap

Corner flap exploits the puckered feature of a ring structure, and involves the movement of a corner ring-atom to the other side of the local average plane. Two to four contiguous dihedral angles are simultaneously changed along the ring. The advantages of corner

flap are:

- it is highly efficient in producing a new energy-minimum
- it can be considered to mimic a barrier-crossing step in the elementary process of thermal conformational interconversion
- it generally does not propagate itself, and can therefore be applied to every ring-atom. In many cases, as many starting structures as the number of ring-atoms can be obtained.

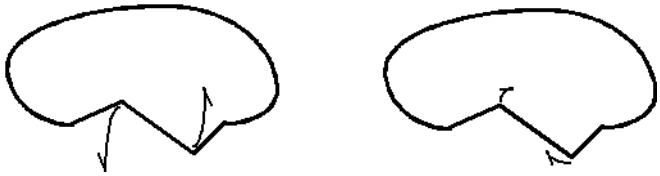


Edge flip

Whilst corner flap is efficient for small to medium ring structures, it is sometimes an unsuccessful technique for larger rings. For example, a ring-atom that is lying on the average local ring plane and flanked by a pair of gauche bonds of the same sign cannot be flapped. Corner flap alone cannot produce all the nearby energy minima for larger rings where mechanisms of conformational interconversion involving more than four contiguous bonds exist.

Edge flip is where two adjacent ring-atoms are simultaneously given the corner flap in opposite directions, where a ring bond is flipped. Edge flip is best illustrated by the chair-to-twist boat conversion of cyclohexane. An edge flip perturbation mode, which proved to be effective for large rings, consists of simultaneous small flapping of two adjacent ring-atoms towards the inside of the ring. In contrast to the other two perturbation methods, both directed towards the outside of the ring, this mode is a local inflection occuring for ring structures with a large cavity space. The edge flip involves rotation of two to five contiguous ring bonds, and are called when certain combinations of three contiguous dihedral angles patterns (A, G, G') appear along the ring. Careful structural adjustments are given in

order to ensure smooth transformation of local structure by edge flip, which is actually a much larger perturbation.



Stepwise rotation

The acyclic part of a molecule is perturbed by stepwise rotation. Typically, a Csp^3-Csp^3 bond is given 120 and -120 rotations to produce a pair of new rotamers. This method, combined with the reservoir-filling strategy for guiding the search direction, searches low-energy conformers for short side chains and linear molecules with up to six to ten rotatable acyclic bonds. However, it is not as effective for large molecules with multiple branching, where unexpectedly high-energy starting structures are produced.

Optimization

Pre-check during optimization

The time required to perform systematic perturbations on the initial structure comprises only a few percent of the total computing time, while by far the most time-consuming step is the geometry-optimization. Therefore, the pre-check is an effective way to increase the efficiency of the conformational space search. In CONFLEX, a structure that is being geometry-optimized is frequently compared with all the stored conformers during the optimization, and that calculation is stopped as soon as the candidate structure is identified as superimposable with one of the stored structures. However, if comparison is made too often, the comparison time will take up a significant part of the total time when the number of stored structures increases. Therefore, with this option, CONFLEX will perform the comparison at 0, 10, 20, and every 10 iterations until 200 iteration, and every 50 iterations thereafter. This strategy reduces the total computing time by 30 to 60 %.

Comparison

Comparison using conformational distance

The similarity between two conformers can be quickly identified by comparing the root mean square of differences in the corresponding pair of dihedral angles, f^A and f^B. This method is fast and accurate. To save time, the dihedral angles of a stored conformer are retrieved for comparison rather than re-calculating those dihedral angles each time.

$$d_{conf} = \sqrt{\left(\sum_{i=1}^{N_{dihedral}} (f_i^A - f_i^B)^2 \right) / N}$$

21 CAChe BioComputations

Overview

This chapter explains the theories and methods behind the following CAChe biocomputations:

- Residue names
- Protein secondary structure
- Dihedral angles used for building peptides
- Sequence property predictions for
  - antigenicity
  - hydrophobicity
  - hydrophilicity
  - flexibility
- Sequence alignment algorithm

Contents

Understanding Residue Names 21-2
Understanding Protein Secondary Structure Definition 21-4
Secondary structure concepts 21-4
Defining secondary structure 21-4
Understanding Dihedral Angles for Building Peptides 21-6
3D structure concepts 21-6
Predefined dihedral angles for regular polypeptide conformations 21-6
Understanding Sequence Property Predictions 21-8
Sequence property concepts 21-8
Sequence property parameters 21-9
Understanding Sequence Alignment 21-12
Alignment concepts 21-12

Understanding Residue Names

Residue names used in CAChe are those defined in the Protein Data Bank Contents Guide: Atomic Coordinate Entry Format Description Version 2.1 (draft), October 25, 1996 ". Amino acids are defined in the following table

Name	3 Letter code	1 Letter code	Formula	Mol. wt.
Alanine	ALA	A	C3 H7 N1 O2	89.09
Arginine	ARG	R	C6 H14 N4 O2	174.2
Asparagine	ASN	N	C4 H8 N2 O3	132.12
Aspartic acid	ASP	D	C4 H7 N1 O4	133.1
ASP/ASN ambiguous	ASX	B	C4 H71/2 N11/2 O31/2	132.61
Cysteine	CYS	C	C3 H7 N1 O2 S1	121.15
Glutamine	GLN	Q	C5 H10 N2 O3	146.15
Glutamic acid	GLU	E	C5 H9 N1 O4	147.13
GLU/GLN ambiguous	GLX	Z	C_5H91/2 N11/2 O31/2	146.64
Glycine	GLY	G	C2 H5 N1 O2	75.07
Histidine	HIS	H	C6 H9 N3 O2	155.16
Isoleucine	ILE	I	C6 H13 N1 O2	131.17
Leucine	LEU	L	C6 H13 N1 O2	131.17
Lysine	LYS	K	C6 H14 N2 O2	146.19
Methionine	MET	M	C5 H11 N1 O2 S1	149.21
Phenylalanine	PHE	F	C9 H11 N1 O2	165.19
Proline	PRO	P	C5 H9 N1 O2	115.13
Serine	SER	S	C3 H7 N1 O3	105.09
Threonine	THR	T	C4 H9 N1 O3	119.12
Tryptophan	TRP	W	C11 H12 N2 O2	204.23
Tyrosine	TYR	Y	C9 H11 N1 O3	181.19
Valine	VAL	V	C5 H11 N1 O2	117.15

The nucleotides are defined in this table.

Name	3 Letter code[a]	1 Letter code	Formula	Mol. wt.
Adenosine	A	A	C10 H14 N5 O7 P1	347.22
Cytidine	C	C	C9 H14 N3 O8 P1	323.20
Guanosine	G	G	C10 H14 N5 O8 P1	363.22
Inosine	I	I	C10 H13 N4 08 P1	348.21
Thymidine	T	T	C10 H15 N2 08 P1	322.21
Uridine	U	U	C9 H13 N2 09 P1	324.18

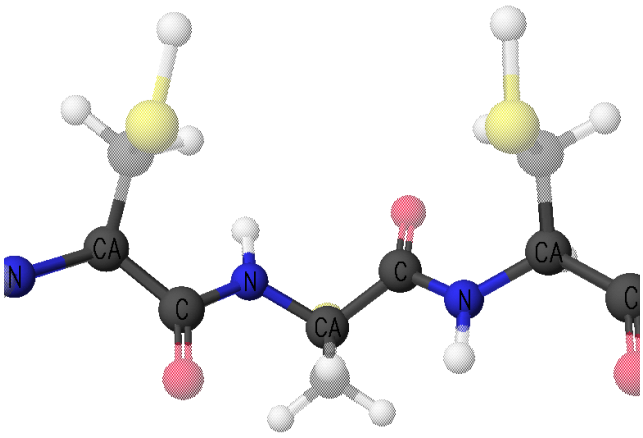
a. When 3-letter codes are displayed in the Sequence View, nucleotides are displayed as single letters.

Understanding Protein Secondary Structure Definition

This section provides reference information about the way CAChe defines secondary structure from the geometry of a protein.

Secondary structure concepts

Regions of proteins can be described as alpha helicies, beta sheets and turns. Alpha helicies and beta sheets are stable structures created by hydrogen bonds and first predicted in 1951 by Linus Pauling and Robert Corey. These regions can be readily observed when proteins are displayed in the CAChe workspace.



Defining secondary structure

CAChe uses hydrogen bonds to classify regions of proteins as helical, beta sheets or turns. Hydrogen bonds are determined by distance criteria between N-H and C=O groups. The method used is that of Kabsch and Sander.[1]

1. Wolfgang Kabsch and Christian Sander, “Dictionary of Protein Secondary Structure: Pattern Recognition of Hydrogen-Bonded and Geometrical Features”, *Biopolymers*, **1983**, *22*, 2577-2637.

This method is the standard method used by the Protein Data Bank for automatic verification and validation of HELIX and SHEET records.

Secondary structure is displayed with 1-letter codes shown in the following table.

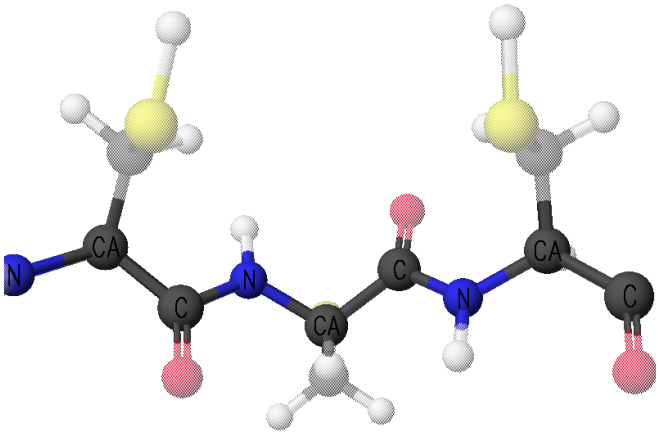
Secondary Structrue Codes	Description
H	Residue is in 4-helix
B	Residue is in isolated beta bridge
E	Residue is in extended strand or participates in beta ladder
G	Residue is in 3-helix
I	Residue is in 5-helix
T	H-bonded turn

Understanding Dihedral Angles for Building Peptides

This section provides reference information about the way CAChe builds peptides.

3D structure concepts

The shape of proteins and peptides is determined largely by the dihedral angles of the backbone. The backbone is defined by PDB atom names. For proteins, the backbone consists of atoms named N, CA and C.



Predefined dihedral angles for regular polypeptide conformations

CAChe uses predefined dihedral angles for protein conformations. The angles are from G. N. Ramachandran and V. Sasisekharan, *Adv. Protein Chem.*, **1968**, *23*, 283 and IUPAC-IUB Commission on Biochemical Nomenclature, *Biochemistry*, **1970**, *9*, 3471.

Structure	Phi	Psi
Fully extended	180	180
Antiparallel beta sheet	-139	+135
Parallel beta sheet	-119	+113

Structure	Phi	Psi
Right-handed alpha helix	-57	-47
Left-handed alpha helix	+60	+60
3_{10} helix	-49	-26
pi helix	-57	-70

Predefined values for turns are from C. M. Wilmot and J. M. Thornton, "Analysis and Prediction of the Different Types of β-Turn in Proteins," *J. Mol. Biol.,* **1968**, *203*(1), 221-32.

Turn	Phi1	Psi1	Phi2	Psi2
Type 1	-60	-30	-90	0
Type 1'	+60	+30	+90	0
Type 2	-60	+120	+80	0
Type 2'	+60	-120	-80	0

Understanding Sequence Property Predictions

CAChe predicts sequence properties for

- antigenicity
- hydrophobicity
- hydrophilicity
- flexibility.

This section provides reference information about the way CAChe predicts sequence properties from the residue sequence using average parameters.

Sequence property concepts

Regions of proteins can be described as antigenetic, hydrophobic, hydrophilic and/or flexible. CAChe uses established, simple algorithms for predicting these properties. The property for each residue depends on its type and the types of neighbor residues in the sequence. The following formula is used

$$P_i = \frac{1}{w} \sum_{j=i-\frac{w}{2}}^{i+\frac{w}{2}} P_j$$

P_i is the average property for residue i; p_j is the property published and shown in the reference tables and w is the window size. The window size is the number of residues included in the average.

Sequence property parameters

Sequence property parameters are defined according to this table.

1 letter code	Antigenicity Hopp and Woods (Hydrophilicity Index)[a]	Antigenicity Parker (Hydrophilicity Index)[b]	Antigenicity Welling[c]	Hydropathy Kyte and Doolittle (Hydrophobicity Index)[d]	Hydrophobicity Sweet, Eisenberg[e]
A	-0.500	2.100	0.115	1.800	-0.400
B	1.600	8.500	0.000	-3.500	-1.115
C	-1.000	1.400	-0.120	2.500	0.170
D	3.000	10.000	0.065	-3.500	-1.310
E	3.000	7.800	-0.071	-3.500	-1.220
F	-2.500	-9.200	-0.141	2.800	1.920
G	0.000	5.700	-0.184	-0.400	-0.670
H	-0.500	2.100	0.312	-3.200	-0.640
I	-1.800	-8.000	-0.292	4.500	1.250
K	3.000	5.700	0.206	-3.900	-0.670
L	-1.800	-9.200	0.075	3.800	1.220
M	-1.300	-4.200	-0.385	1.900	1.020
N	0.200	7.000	-0.077	-3.500	-0.920
P	0.000	2.100	-0.053	-1.600	-0.490
Q	0.200	6.000	-0.011	-3.500	-0.910
R	3.000	4.200	0.058	-4.500	-0.590
S	0.300	6.500	-0.026	-0.800	-0.550
T	-0.400	5.200	-0.045	-0.700	-0.280
V	-1.500	-3.700	-0.013	4.200	0.910
W	-3.400	-10.000	-0.114	-0.900	0.500
X	-0.200	0.000	0.000	-0.490	0.000
Y	-2.300	-1.900	0.013	-1.300	1.670
Z	1.600	6.900	0.000	-3.500	-1.065
Default Window size (*w*)	7	7	19	19	19

a. Hopp, T.P. and Woods, K.R., *Proc. Natl. Acad. Sci. USA*, **1981**, *78*, 3824-3828
b. Parker, J. M., Guo, D., Hodges, R. S., *Biochemistry*, **1986**, *25*, 5425-5432

c. Welling, G.W., Weijer W.J., van der Zee, R., Welling-Wester, S., *FEBS Lett*., **1985**, *188*, 215-218
d. Kyte, J. and Doolittle, R. F., J. Mol. Biol., **1982**, *157*, 105-132
e. Sweet, R. M. and Eisenberg, D., J. Mol. Biol., **1983**, *171*, 479-488

.

1 letter code	Hydrophobicity Janin[a]	Hydrophobicity Fauchere and Pliska[b]	Hydrophobicity Manvalan[c]	Hydrophilicity Goldman, Engelman, Steitz[d]
A	0.300	0.31	12.97	-1.600
B	-0.550	-0.68	11.13	7.000
C	0.900	1.54	14.63	-2.000
D	-0.600	-0.77	10.85	9.200
E	-0.700	-0.64	11.89	8.200
F	0.500	1.79	14	-3.700
G	0.300	0	12.43	-1.000
H	-0.100	0.13	12.16	3.000
I	0.700	1.8	15.67	-3.100
K	-1.800	-0.99	11.36	8.800
L	0.500	1.7	14.9	-2.800
M	0.400	1.23	14.39	-3.400
N	-0.500	-0.6	11.42	4.800
P	-0.300	0.72	11.37	0.200
Q	-0.700	-0.22	11.76	4.100
R	-1.400	-1.01	11.72	12.300
S	-0.100	-0.04	11.23	-0.600
T	-0.200	0.26	11.69	-1.200
V	0.600	1.22	15.71	-2.600
W	0.300	2.25	13.93	-1.900
X	0.000	0.000	0	0.000
Y	-0.400	0.96	13.42	0.700
Z	-0.700	-0.43	11.82	6.150
Default Window size (*w*)	19	19	19	19

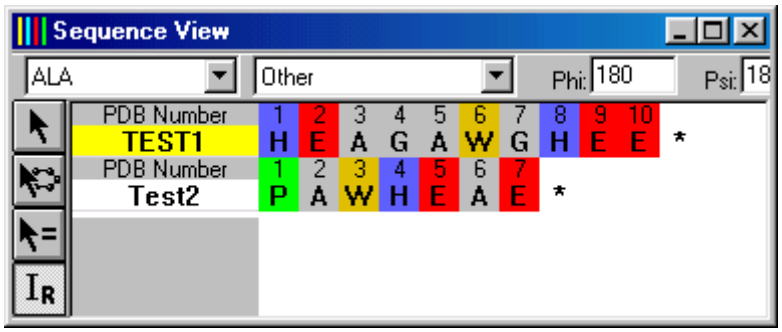
a. Janin, J., *Nature*, **1979**, *277*, 491
b. Fauchere, J. L. and Pliska, V., *Eur. J. Med. Chem. - Chim. Ther.*, **1983**, *18*, No. 4, 369-375
c. Manvalan, P. and Ponnuswamy, P. K., *Nature,* **1978***, 275*, 673
d. Karplus, P.A. and Schulz, G. E., Naturwissenschaften, **1978**, *72*, 212-213

Understanding Sequence Alignment

CAChe aligns two sequences by performing a pairwise global alignment using the Needleman-Wunsch algorithm[1] with a BLOSUM50 substitution matrix.

Alignment concepts

When sequences from two proteins are placed in adjacent rows, it is

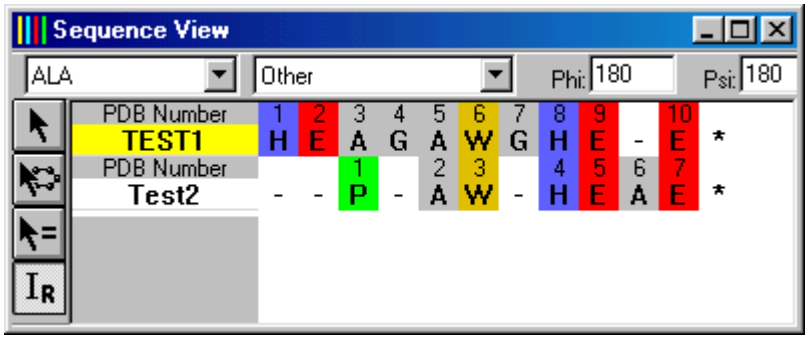


Sequences before alignment

likely that some residues in one sequence will be identical to the residues at the same position in the other sequence. In some cases the adjacent residues will be similar in properties and function and frequently substituted during evolution. In other cases, the number

1. Needleman, S. B., and Wunsch, C. D., *J. of Mol. Bio.*, **1970**, *48*, 443-453, “A general method applicable to the search for similarities in the amino acid sequence of two proteins”.

of matching residues can be increased by inserting “gaps” in the sequence that account for evolutionary insertions and deletions.



Sequences after alignment

Alignment is the process of inserting gaps so that the score of adjacent residues is maximized. The scoring used in CAChe is the BLOSUM50 substitution matrix augmented with a single column of

weights for any group that is not a standard amino acid.. The

BLOSUM50 Substitution Matrix Used in CAChe

	A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V	?
A	**5**	-2	-1	-2	-1	-1	-1	0	-2	-1	-2	-1	-1	-3	-1	1	0	-3	-2	0	-1
R	-2	**7**	-1	-2	-4	1	0	-3	0	-4	-3	3	-2	-3	-3	-1	-1	-3	-1	-3	-1
N	-1	-1	**7**	2	-2	0	0	0	1	-3	-4	0	-2	-4	-2	1	0	-4	-2	-3	-1
D	-2	-2	2	**8**	-4	0	2	-1	-1	-4	-4	-1	-4	-5	-1	0	-1	-5	-3	-4	-1
C	-1	-4	-2	-4	**13**	-3	-3	-3	-3	-2	-2	-3	-2	-2	-4	-1	-1	-5	-3	-1	-1
Q	-1	1	0	0	-3	**7**	2	-2	1	-3	-2	2	0	-4	-1	0	-1	-1	-1	-3	-1
E	-1	0	0	2	-3	2	**6**	-3	0	-4	-3	1	-2	-3	-1	-1	-1	-3	-2	-3	-1
G	0	-3	0	-1	-3	-2	-3	**8**	-2	-4	-4	-2	-3	-4	-2	0	-2	-3	-3	-4	-1
H	-2	0	1	-1	-3	1	0	-2	**10**	-4	-3	0	-1	-1	-2	-1	-2	-3	2	-4	-1
I	-1	-4	-3	-4	-2	-3	-4	-4	-4	**5**	2	-3	2	0	-3	-3	-1	-3	-1	4	-1
L	-2	-3	-4	-4	-2	-2	-3	-4	-3	2	**5**	-3	3	1	-4	-3	-1	-2	-1	1	-1
K	-1	3	0	-1	-3	2	1	-2	0	-3	-3	**6**	-2	-4	-1	0	-1	-3	-2	-3	-1
M	-1	-2	-2	-4	-2	0	-2	-3	-1	2	3	-2	**7**	0	-3	-2	-1	-1	0	1	-1
F	-3	-3	-4	-5	-2	-4	-3	-4	-1	0	1	-4	0	**8**	-4	-3	-2	1	4	-1	-1
P	-1	-3	-2	-1	-4	-1	-1	-2	-2	-3	-4	-1	-3	-4	**10**	-1	-1	-4	-3	-3	-1
S	1	-1	1	0	-1	0	-1	0	-1	-3	-3	0	-2	-3	-1	**5**	2	-4	-2	-2	-1
T	0	-1	0	-1	-1	-1	-1	-2	-2	-1	-1	-1	-1	-2	-1	2	**5**	-3	-2	0	-1
W	-3	-3	-4	-5	-5	-1	-3	-3	-3	-3	-2	-3	-1	1	-4	-4	-2	**15**	2	-3	-1
Y	-2	-1	-2	-3	-3	-1	-2	-3	2	-1	-1	-2	0	4	-3	-2	-2	2	**8**	-1	-1
V	0	-3	-3	-4	-1	-3	-3	-4	-4	4	1	-3	1	-1	-3	-2	0	-3	-1	**5**	-1
?	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	**1**

implementation of the Needleman-Wunsch algorithm follows that of Gotoh[1] as described by Durbin, *et al.*[2]

The Needleman-Wunsch global alignment gives the highest scoring alignment. However, it may not be unique. There may be other alignments with the same score.

If the two sequences are of length *n* and *m* respectively, then the time and memory required for the alignment are proportional to *nm*. For protein sequences that are typically less than 1,000 residues long, alignment is quick.

1. Gotoh, O., *J. of Mol. Bio.*, **1996**, *264*, 823-838, “An improved algorithm for matching biological sequences”.
2. Durbin, R., Eddy, S. R., Krough, A., Mitchison, G., “Biological sequence analysis: Probabilistic models of proteins and nucleic acids”, Cambridge University Press, **1998**, 19-22.

Part five

Appendices

The following appendices describe the shortcuts you can use in CAChe, and the files that are added to your computer when you install your CAChe product:

Appendix A, "*Keyboard and Toolbar Shortcuts*", describes the keyboard shortcuts and commands you can use in CAChe, and describes each button in the toolbar.

Appendix B, "*CAChe File Management*", lists the directory structure and file content of your `Cache` folder.

A Keyboard and Toolbar Shortcuts

Overview

This appendix contains details of:

- keyboard shortcuts and the corresponding toolbar buttons that replace menu options
- keyboard commands that provide operations for which there are no menu options
- toolbar buttons and the menu options that each button performs.

Contents

Keyboard shortcuts **A-2**
Menu option shortcuts A-3
Miscellaneous keyboard commands A-4
Toolbar shortcuts **A-6**

Keyboard shortcuts

Keyboard commands and toolbar buttons are available as shortcuts for some menu options. Some keyboard shortcuts provide operations not available through menus or dialog boxes.

Keyboard shortcuts and their corresponding toolbar buttons are shown on the following pages, alongside the menu options that the shortcut or toolbar button performs. Also, miscellaneous other keyboard commands are summarized.

Menu option shortcuts

Keys	Action	Menu option	Toolbar button
Ctrl N	Create new (blank) file.	**File | New**	
Ctrl O	Open an existing file.	**File | Open**	
Ctrl Z	Undo (or redo) last operation.	**Edit | Undo**	
Ctrl S	Save active file.	**File | Save**	
Alt F4	Quit application.	**File | Exit**	
Ctrl P	Print active window.	**File | Print**	
Ctrl F	Scale and center a chemical sample.	**View | Fit in Window**	
Ctrl C	Copy selected items to clipboard.	**Edit | Copy**	
Ctrl X	Cut selected items to clipboard.	**Edit | Cut**	
Ctrl V	Paste selected items into active workspace.	**Edit | Paste**	
Del	Delete selected items.	**Edit | Delete**	
Ctrl D	Duplicate selected items.	**Edit | Duplicate**	
Ctrl L	Add a label to selected items.	**Adjust | Define Geometry Label**	
Ctrl K	Connect two selected atoms with a bond.	**Edit | Connect Atoms**	

Appendices

Keys	Action	Menu option	Toolbar button
Ctrl A	Select all.	**Edit | Select All**	
Ctrl I	Invert chiral carbon.	**Edit | Invert Chirality**	

Miscellaneous keyboard commands

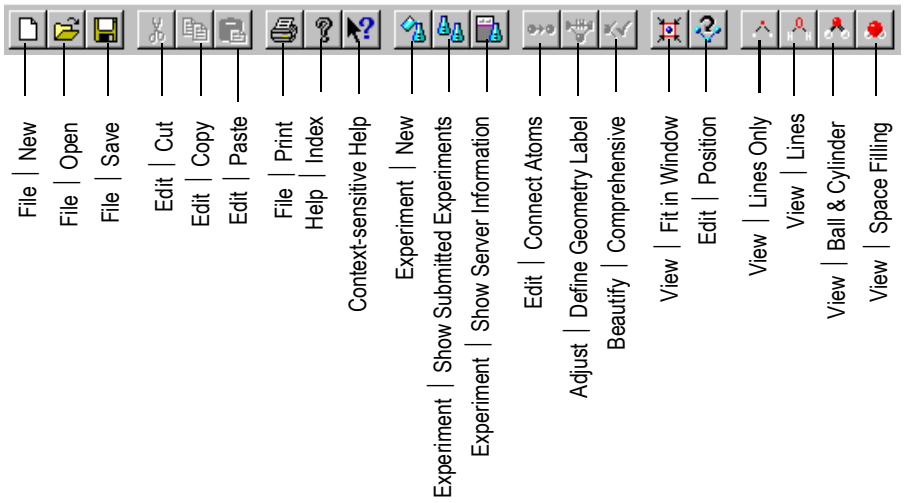
The following keyboard commands are available for miscellaneous functions.

Keys	Action
n or **N**	Exit all keyboard modes, keys no longer manipulate your chemical sample or.
+	Increase the rate of change for keyboard view adjustments like rotating, translating, and scaling.
-	Decrease the rate of change for keyboard view adjustments like rotating, translating, and scaling.
space	Toggle the autorepeat flag. When on, autorepeat continues a viewing adjustment such as rotate until another viewing command is received.
i or **I**	Return view of molecular structure to initial conditions, including no rotation or translation, scale factor of 0.1, and x, y, and z axes aligned with origin.
a or **A**	Enter the keyboard view rotation mode and set the rate of change to 90° per rotation. No adjustments occur until you choose a direction of rotation (x, X, y, Y, z, Z).

Keys	Action
r or **R**	Enter the keyboard view rotation mode. No adjustments occur until you choose a direction of rotation (x, X, y, Y, z, Z).
t or **T**	Enter the keyboard view translation mode. No adjustments occur until you choose a direction of translation (x, X, y, Y, z, Z).
s or **S**	Enter the keyboard view scale mode. No adjustments occur until you choose a direction of scaling (x, X, y, Y, z, Z).
x	Assign a negative x direction to the current view adjustment mode. Rotate about minus x axis. Translate in the negative x direction. Decrease scale.
X	Assign a positive x direction to the current view adjustment mode. Rotate about positive x axis. Translate in the positive x direction. Increase scale.
y	Assign a negative y direction to the current view adjustment mode. Rotate about minus y axis. Translate in the negative y direction. Decrease scale.
Y	Assign a positive y direction to the current view adjustment mode. Rotate about positive y axis. Translate in the positive y direction. Increase scale.
z	Assign a negative z direction to the current view adjustment mode. Rotate about minus z axis. Translate in the negative z direction. Decrease scale.
Z	Assign a positive z direction to the current view adjustment mode. Rotate about positive z axis. Translate in the positive z direction. Increase scale.

Toolbar shortcuts

The following diagram shows the menu commands that each toolbar button performs.



B CACHe File Management

Overview

This appendix contains details of:

- the files and folders added to your hard disk when you install CACHe from the installation CD-ROM.

Contents

CACHe folders and files **B-2**

CAChe folders and files

The table below lists the files and folders that are added to your computer when you install your CAChe product. The files and folders that are installed depend on the particular CAChe product that you have purchased.

Folder	File name	Description
c:\CACHE		
	cache.exe GenID.exe MessageDirector.exe PLWin.exe ProcedureEditor.exe	• CAChe applications
	Analysis.idx SamplePart.idx	• Property and procedure index
	Space-Groups	• Space group transformations
	het_dictionaryCIF.txt	• HET group definitions from PDB
	Datadict	• Data dictionary
	cache.chm cache2.chm cache.cnt cache2.cnt cache.hlp cache2.hlp cache_pe.cnt	• CAChe Help files
	ReleaseNotes.pdf Tutorials.pdf UserGuide.pdf	• CAChe documentation
		• Various resource files and libraries used by cache.exe, PLWin.exe, and ProcedureEditor.exe
c:\CACHE\APP		
	errdll.dll	• Error code resource
	Crystal.dll	• Crystal code resource

Folder	File name	Description
c:\CACHE\BIN		
	CalcMgr.exe	CAChe Calculation Manager
c:\CACHE\BIN\CONFLEX		• Contains Conflex compute engine and Conflex manager
c:\CACHE\BIN\DYNAMICS		• Contains Dynamics compute engine and Dynamics manager
c:\CACHE\BIN\MECHANICS		• Contains Mechanics compute engine and Mechanics manager
c:\CACHE\BIN\MOPAC		• Contains MOPAC compute engines and MOPAC manager
c:\CACHE\BIN\TABULATOR		• Contains Tabulator compute engine and Tabulator manager
c:\CACHE\ExpEnvironment\Data		
c:\CACHE\ExpEnvironment\Modules		
c:\CACHE\ExpEnvironment\Packages		
c:\CACHE\FragmentLibrary		• Chemical sample files
c:\CACHE\InstallationNotes		• CAChe installation documents
c:\CACheUser\cachetmp		• Calculation queue and files while calculations are running
c:\CACheUser\ExpEnvironment		• User procedure packs
c:\CACHE\XLATORS		
	cachemap.dll cachetrn.dll crystalstructure.dll fio.dll gaussian.dll pdbio.dll ShelX.dll	• Translation libraries used during file input and output

I

Index

Overview

This is a full index for the BioMedCAChe User Guide.

Symbols

.csf files 4-3
.ins files 6-65
.seq files
    generating 20-5
.xsf files 6-64

Numerics

310 helix 21-7
3D cursor 3-15

A

Adding chemical samples in ProjectLeader 12-12
Adjusting atom distance 8-13
Agouti-related protein 19-22
All conformations dialog box 14-27
Allinger, N. L. 20-3
Alpha helix 21-7
Amino acid
    creating nonstandard 9-47
    nonstandard 9-45
Amino acid repository 9-45
Analysis criteria 14-24
Analyzing map files 14-22
Angle
    bond 8-14
    dihedral 8-15
    improper torsion 8-17
Animate geometry labels dialog box 8-44
Animating
    map files 14-26
    search labels 8-44
Application window 3-4
Arrow buttons 3-24
Assemblage file 20-6
Atom attributes dialog box 5-21, 6-13, 8-2, 8-33, 9-7, 16-8
Atom properties 10-7
    changing 5-19
Atom/bond tool 3-14, 3-19, 3-32, 4-4
Atomic partial charge 2-15, 10-7
Atoms
    calculating partial charge 16-2
    change the charge of 5-21
    changing the appearance of 6-8
    changing the color of 6-14
    changing the radius 5-26
    changing the shape of 6-11, 6-13
    color 16-10
    displaying 6-18
    drawing 4-5
    fusing 7-21
    grouping 7-24
    hiding 6-18
    hiding locked labels 8-33
    interpreting properties 16-7
    labeling 6-8
    labels 16-8
    lock 8-32
    measuring distance 8-13
    modifying 5-2
    properties 16-1
    selecting locked atoms 8-34
    specifying distance 8-13
    ungroup 7-28
    unlock 8-33
Axis attributes
    changing 14-18
Axis attributes dialog box 14-18

B

Beautify menu 5-24, 5-25, 5-26
Beta sheet 21-6
BioComputations 21-1
Biomolecules 9-1
    investigating 19-1
Bond attributes dialog box 6-24, 16-11
Bond order 2-15, 10-7

Bond orders 20-11
Bond properties 10-7
    changing 5-19
Bond strain 2-15, 10-7, 15-14
bond type 3-9
Bond Type box 3-12
Bond types 5-32
Bonds
    calculating order 16-4
    calculating properties 16-4
    calculating strain 16-5
    changing 5-28
    changing the appearance of 6-21
    changing the color of 6-25, 6-26
    changing the shape of 6-21
    changing type 5-30
    color 15-14
    coordinate covalent 5-33
    displaying 6-28
    double covalent 5-32
    drawing 4-6
    drawing between two exisiting atoms 4-7
    drawing with an atom 4-8
    fusing 7-22
    hiding 6-28
    interpreting properties 16-7
    ionic 5-33
    modifying 5-2
    order 15-14, 15-15, 16-7, 16-11
    π coordination bond 5-34
    properties 16-1
    radius 16-11
    single covalent 5-32
    specifying angle 8-14
    strain 15-14, 16-12, 16-13
    triple covalent 5-33
    type 15-14, 15-15
    weak 5-33
Broken geometry locks 8-31
Bumps
    labeling 8-28
Buttons
    toolbar A-1, A-3

C

CAChe
    overview 2-2
    quitting 3-45
    sequence view 9-20
    user interface 3-3
    workspace 3-8
Calculating
    atomic partial charge 16-2
    bond order 16-4
    bond properties 16-4
    connectivity indexes 12-2
    current energy 13-11
    dipole vectors 12-2
    RMS error 8-10
    using classical mechanics 13-11
    using quantum mechanics 13-11
Calibrating CAChe 2-9
Calibrations
    establishing 2-18, 12-2
Calling a procedure 11-20
Center of rotation (rotate tool) 7-4
Centering objects 7-6
Changing
    atom or bond properties 3-42
Changing a bond 5-28
Changing atom and bond properties 5-19
Charge 16-7
    changing 5-21
Charge box 3-9, 3-11
Check boxes 3-24
Chemical sample files 4-2
    opening existing 4-3
    opening in ProjectLeader 12-12
    opening new 4-2
    preparing 10-4
Chemical samples
    creating 4-1
    modifying 5-1
    optimizing 13-1
    properties 10-5
    viewing 6-1

Chiral centers 8-1, 8-2
inverting 8-3
labeling 8-2
viewing 8-2
Choosing options and items 3-17
Classical mechanics 2-4, 13-3
rigid energy map 14-6
Clicking and dragging on objects 3-19
Clicking on objects 3-18
Cloning an experiment 11-27
Closing ProjectLeader 12-45
Color 15-14, 15-15, 16-11
atom 6-14, 16-10
bond 15-14
changing bonds 6-25
default 15-13
define custom palette 6-42
elements 6-37
geometry labels 8-25
partial charge and MO polarity 15-13
surfaces 15-13
tables 15-13
threshold values 15-12
Color dialog box 6-41
Color index 15-14
Color palette
changing 6-41
editing 6-38
view 6-40
Comments, adding 12-21
Completing molecules 4-9
Comprehensive command (Beautify menu) 4-15
Computational applications 20-1
Computational chemistry 2-8
Compute engine data
editing 11-23
Computer-aided chemistry
accuracy 2-10
an overview 2-7
CONFLEX 2-21, 20-23
Conformation properties 10-8
Conformation text box 8-45
Conformational analysis window 14-22
Conformations 14-9
low-energy 14-1
Connectivity indexes 12-2
Coordinate covalent bonds 5-33
Copy objects to other Windows applications 7-16
Copying objects 7-14
Copying objects from ChemDraw/ISIS Draw 7-17
Copying sample properties 12-18
COSMO 20-19
Creating
a group package 11-31
chemical samples 4-1
experiments 11-25
Crystal Shape dialog box 6-55
Crystal structures
building a molecular crystal 6-60
building an infinite lattice 6-62
building asymmetric atoms 6-60
creating CrystalStructure files 6-63
defining cell parameters 6-57
defining fractional coordinates 6-58
displaying and hiding crystal boundaries 6-63
importing data from a text file 6-65
selecting a space group 6-55
ShelX files 6-65
Current energy 2-14, 10-6
calculating 13-11
Cutting objects 7-18

D

Define charge dialog box 5-27
Define custom colors 6-42
Defining
atom groups 7-24
search labels 8-41
Delete
geometry labels 8-26
hydrogens 4-15
molecule portions 7-18
objects 7-19

Density 15-16
Deselecting
more than one object 5-6
one object 5-5
similar atoms 5-11
Details buttons 3-26
DGauss 2-22
Dialog boxes
using 3-22
Dielectric energy 12-3
Dihedral angle
specifying 8-15
Dihedral search labels 8-41
Dipole moments 12-3, 20-11
Dipole vectors
calculating 12-2
x, y, and z 12-3
Directory buttons 3-25
Display options 6-2
ball and cylinder 6-3
lines 6-2
lines only 6-2
partial charge and calculated bond order 6-3
space filling 6-3
surfaces 15-18
Displaying
bonds 6-28
electrons 6-16
experimental details 10-35
sample properties 12-17
servers 10-33
Workspace from ProjectLeader 12-14
Distance
changing the workspace distance 6-44
specifying within molecules 8-12
Distribution of electrons 15-1
Docking
ligands into proteins 19-22
Document windows
arranging 3-16
Documentation set 1-2
Double covalent bonds 5-32
Double-clicking items 3-20
Draw atom/bond tool 3-30
Drawing
a bond with an atom 4-8
atoms 4-5
bonds 4-6
bonds between two existing atoms 4-7
molecules 4-4
Drawing settings 6-43
Drawing settings dialog box 6-43
Drawing tools 2-3
Drop-down lists 3-27
Duplicating
molecules 7-13
objects 7-13
Dynamic reaction coordinate 17-4, 20-19
Dynamics 20-7
generating trajectories 20-9
trajectory 2-16, 10-8, 14-10
Dynamics application 2-21

E

Edit
color palette 6-38
parameter data 11-30
procedures 11-17
sample properties 12-18
settings of a compute engine 11-23
Electron affinity 12-3, 15-7
Electron density 2-14, 10-6, 15-13, 15-15
colored by electrostatic potential 15-3
Electron density surface 15-2
colored by superdelocalizability 15-5
colored by susceptibility 15-4
Electron distribution 15-1
Electronic
properties 2-8
spectra 18-6
Electrons
displaying 6-16
hiding 6-16
view settings 6-48

Electrostatic potential 10-7, 15-3, 15-18
Electrostatic potential surface 15-6
Element and size limitations 10-31
Element color
  changing 6-37
Element type box 3-9, 3-10, 4-5
Energy 10-6
  calculating 13-11
  molecular mechanics 20-2
Energy maps
  creating with mechanics 20-5
  generating 14-2
  optimizing 14-7
  rigid 14-6
Enzymes 13-8
Exit. *See* Quitting
Experiment dialog box 10-23
Experiment environment
  managing the 11-8
  refreshing the 11-35
Experiment status dialog box 10-27
Experiments 10-2
  atom 2-15
  bond 2-15
  chemical sample 2-14
  chemical sample conformation 2-15
  cloning 11-27
  creating 11-25
  displaying details 10-35
  displaying servers 10-33
  importing 11-28
  performing 2-12, 10-1
  reaction 2-16
  running 10-18
  running a ProjectLeader experiment 12-20
  running simultaneously 10-26
  saving files 10-23
  setting up 10-4
  stopping 10-24
  troubleshooting 10-32
  viewing 10-27
  workspace 2-13
Experiments submitted dialog box 10-25, 10-29
Exporting
  experiment components 11-37
  ProjectLeader worksheet 12-43
  scatter plots 12-31

F

Faster motion mode 7-12
File management B-1
Files B-1, B-2
  experimental 10-36
  generation of output files 10-32
  log 10-40
  opening saved files 4-20
  output 10-40
  printing 4-22
  saving 4-17
  saving experiments 10-23
Find reaction paths 2-17
  experiment 17-1
Folders B-1, B-2
  sample.io 10-37
  sample.iso 10-37
Footnotes 12-37
Forward stepwise regression 12-3
Frontier
  density 2-14, 15-16
  orbitals 10-6
Fuse
  atoms 7-21
  bonds 7-22
  ring structures 7-21

G

Generating energy maps 14-2
  rigid 14-6
Geometry
  broken locks 8-31
  correcting 4-14

disabling locks 8-35
investigating molecular 8-1
label wizard 8-41
labels 8-40
optimization 2-8
repairing broken locks 8-31
Geometry label attributes dialog box 8-22, 8-25
Geometry label wizard dialog box 8-42
Geometry labels 8-19, 8-24
changing 8-21
changing color 8-25
deleting 8-26
hiding 8-22
hiding text 8-23
locking 8-29
Graph
attributes 14-20
changing color 14-17
Graph attributes dialog box 14-16
Group packages 11-31
Grouping atoms 7-24
Groups
defining 7-24
selecting 7-25, 7-28, 7-29
GroupServer 10-34

H

H-bond
labeling 8-27
Heat of formation 2-14, 10-5, 12-3, 20-13
HELIX 21-5
het_dictionaryCIF.txt 9-3
Hiding
atoms 6-18
bonds 6-28
electrons 6-16
surfaces 15-10
text in geometry label 8-23
HOMO 10-6, 12-3, 18-7
HOMO -5 to LUMO +4 energies
calculating 15-8
HOMO and LUMO 2-14
HOMO and LUMO energies
calculating 15-7
Homolog
creating 19-15
GPCR 19-15
Hybridization
changing 5-20
changing an atoms 5-24, 5-25
correcting 4-13
Hybridization box 3-9, 3-11, 4-5
Hydrogen atoms
hiding 6-19
Hydrogens
deleting 4-15
hiding 6-19
view settings 6-48

I

Identifying procedure numbers 10-9
Import MDL SD files dialog box 12-13
Importing an experiment 11-28
Improper torsion angles
specifying 8-17
Infra-red spectra 18-2
Insert residue tool 9-25
Installation B-1
Interpreting surface color 15-11
Intrinsic reaction coordinate 17-4, 20-19
Inverting chiral centers 8-3
Investigating
atom and bond properties 16-1
electron density surfaces 15-2
electron distribution 15-1
low-energy conformations 14-1
molecular geometry 8-1
molecular orbital energies 15-7
peptide conformations 19-3
reaction path structures 18-2
reactions 17-1
transition state structures 17-2

Ionic bonds 5-33
Ionization energy 15-7
IR transitions 10-6
IR Transitions window 18-3
Isosurfaces 15-17

K

Keyboard
    commands A-4
    shortcuts A-1, A-2
Kinetic energy 17-4

L

Label chiral centers 8-2
Label Wizard
    geometry 8-41
Labels 15-21
    atom 8-33, 16-8
    atoms 6-8
    geometry 8-19, 8-24, 8-29
    in scatter plots 12-29
    search 8-37, 8-43
Legends 15-16
Ligand
    docking 19-22
Limitations
    size and element 10-31
Locked geometry
    disabling 8-35
Locking
    atoms 8-32
    geometry labels 8-29
Locks
    geometry 8-31
Low-energy structures 10-5
LUMO 10-6, 12-3, 18-7

M

Manipulating
    molecules 7-1, 7-9
    search labels 8-43
Manipulation tools 7-2
Map file windows 14-12
Map files
    analyzing 14-22
    animating 14-26
    display options 14-15
    open 14-12
    saving 14-30
Map reaction 2-16, 17-1
Maps
    energy 14-2
Matching properties to procedures 10-15
Matching selections 9-40
MC4R 19-15, 19-22
Mechanics 20-5
    classical 13-3
    concepts 20-2
    optimizing with 20-3
    quantum 13-3, 13-4
Mechanics application 2-21
Melanocortin-4 receptor (MC4R) 19-17
Melanocortin-4 recptor (MC4R) 19-15
Menu bar 3-4
    using 3-20
Menu option 3-20
    shortcuts A-3
Minimum-energy geometries 20-17
Mirroring molecules 8-5
MM
    multiple passes 20-6
    one pass 20-6
MM2 20-3
MO polarity 15-14
Model types 6-4
Modeling
    solvent effects 20-19
    styles 2-3
Modifying

atoms and bonds 5-2
chemical samples 5-1
Molecular connectivity index 12-3
Molecular formula 12-3
Molecular geometry
investigating 8-1
Molecular orbital energies 15-7
calculating 15-8
Molecular orbitals 2-14, 10-6, 15-17, 20-11
color 15-13
surfaces 18-6
Molecular refractivity 12-3
Molecular weight 12-3
Molecules
comparing biomolecules 9-39
completing 4-9
deleting portions 7-18
deselecting 5-8
drawing 4-4
duplicating 7-13
manipulating 7-1, 7-9
mirroring 8-5
optimizing portions 13-6
perfecting 4-10
selecting 5-7
specifying angles and distances 8-12
superimposing 8-6
MOPAC 2-21, 20-11, 20-12
limitations 20-14
Motion Dynamic Models
Simulation 2-9
Motion vectors, displaying 18-2
Mouse actions 3-17
choose 3-17
click 3-18
click and drag 3-19
double-click 3-20
select 3-17
Moving objects 7-6, 7-7
in the workspace 5-5
Multiple pass search 14-9, 20-6
Multiple windows 6-32
Mutual orientations 13-8

N

Navigator window 11-4
New geometry labels 8-37
New users, important information 1-2
Non-scrolling
lists 3-28
windows 3-29
Notes icon 1-6

O

Objects
copying 7-14
cutting 7-18
deleting 7-19
duplicating 7-13
moving 7-6
rotating 7-4
scaling 7-7
zooming in and out 7-8
Octanol-water partitition coefficient 12-3
One pass search 14-9
Online Help 3-43
context-sensitive Help 3-43
the Help system 3-44
Open dialog box 4-3
Opening
a ProjectLeader project 12-11
chemical samples in ProjectLeader 12-12
saved files 4-20
Optimization
selective 13-6
Optimized geometry 2-14, 12-3
Optimized map 2-16, 10-8
Optimized structures
viewing 13-10
Optimizing
chemical samples 13-1, 13-2
energy maps 14-7
geometry 10-5

molecule portions 13-6
quantum mechanics 13-4
using classical mechanics 13-3
Optimum geometry 20-3, 20-11
Orbital energies 15-7
Orbital surfaces, displaying 18-6
Orbitals 15-17
Original Settings command 11-36
Output files 10-21
generation 10-32

P

π coordination bond 5-34
Packages
loading new packages 11-33
Page orientation 4-24
Paper
size 4-25
source 4-25
Parameter bar 14-14
hiding 14-16
Parameter data
editing 11-30
Parameter Data window 11-7
Partial charge 15-14, 16-7, 16-10, 16-11, 20-11
color 15-13
Path
reaction 10-9
Peptide
building 19-3
conformations 19-3
generating 19-6, 19-8
Perfecting molecules 4-10
Performing experiments 10-1, 12-1
Periodic table dialog box 4-11
Periodic table settings dialog box 4-11, 5-27, 6-37
Perspective
changing 6-44
Phi and Psi angle box 9-21
Phi and Psi boxes 9-23
Pi helix 21-7
Plotting
a scatter plot 12-27
variables along an axis 14-16
Polarity 15-14
Polyatomic molecules 20-8
Potential energy maps
exhaustive versus sequential 20-6
Potential energy surface 20-3
Potential polarity 15-14
Previewing printouts 4-22, 12-43
Print
preview (File menu) 4-22
Print dialog box 4-25
Print Setup dialog box 4-23
Print to File dialog box 4-27
Printing
a CAChe window 4-25
files 4-22
options 4-23
orientation 4-24
print to a file 4-27
scatter plots 12-32
Procedure Editor 2-19, 11-1
overview 11-2
quitting 11-38
starting 11-3
Procedure window 11-6
Procedures
adding a step 11-19
calling a procedure 11-20
deleting a step 11-19
identifying numbers 10-9
matching properties 10-15
modifying procedures 11-17
moving a step 11-19
property investigation 10-9
running a procedure 11-21
table 10-10
viewing a step 11-20
ProjectLeader
overview 12-2
printing 12-40

projects 12-11
quitting 12-45
Sample Properties table 12-17
scatter plots 12-27
starting 12-5
ProjectLeader workbook 12-7
adding a chemical sample 12-12
adding a property, sample component, analysis, or comment 12-21
adding footnotes 12-37
components of 12-7
copying objects from ChemDraw, ISIS Draw, or Kekule 12-15
displaying chemical samples as line drawings 12-33
exporting as an .sdf file 12-43
hiding column or row buttons 12-37
selecting a server 12-24
selecting cells 12-24
sorting rows 12-34
viewing cell details 12-39
Properties
atom 10-7
available properties 11-14
bond 10-7
conformation 10-8
matching to procedures 10-15
Sample properties 12-17
showing properties 11-13
Property class
choosing 10-5
Protein
accessible surface 9-13
adjacent surface - pocket 9-15
backbone
N-C-C trace 9-10
selecting 9-9
coloring residues 9-8
crevice surface 9-13
docking 19-22
ribbons 9-10
Protein Data Bank 21-5
Proteins
docking ligandsDocking
ligands into proteins 19-22

Q

QSAR relationships
establishing 2-18, 12-2
QSPR relationships
establishing 2-18, 12-2
Quantum mechanics 13-3
optimized energy map 14-8
optimizing molecules 13-4
rigid energy map 14-7
Quitting
CAChe 3-45
Procedure Editor 11-38
ProjectLeader 12-45

R

Radio buttons 3-25
Radius
bond 16-12
Ramachandran 21-6
Reaction path 10-9
structures 17-4
structures that conserve kinetic energy 17-4
structures without kinetic energy 17-4
Reaction pathways 2-9, 20-11
Reaction properties 10-5, 10-8
Reactions
investigating 17-1
Reactive sites
investigating on enzyme surface 13-8
Refine transition experiment 17-1
Refine transition state 2-17, 10-9
Regression
forward stepwise regression 12-3
multiple linear regression 12-3
reverse stepwise regression 12-3

Repairing broken geometry locks 8-31
Residue tool 9-25
Residue type box 9-21, 9-22
Reverse stepwise regression 12-3
Reversing a coordinate bond 5-31
RGB values 15-14
Rigid energy map 14-6
Rigid map 10-8
Ring
  count 12-3
  size 12-3
Ring geometry
  correcting 4-13
Ring structures
  fusing 7-21
Rotate tool 3-14, 3-30, 3-32, 3-38, 7-2, 7-3
Rotating objects 7-4
Rotation
  defining center for rotate tool 7-4
Rotation settings dialog box 7-5
Rules for the selection tools 5-4
Running
  a procedure 11-21
  experiments simultaneously 10-26
  ProjectLeader experiments 12-20

S

Saddle points 20-17
Sample properties
  copying 12-18
  editing 12-18
  Sample Properties table 12-17
  viewing 12-17
Sample Properties table 12-17
Sample.io folder 10-37
Sample.iso folder 10-37
Save as dialog box
  4-17
Saving
  experiment files 10-23
  files 4-17, 4-19
  map files 14-30
  settings 6-51
Scale tool 3-14, 3-30, 3-33, 3-39, 7-2, 7-8
Scaling
  a scatter plot 12-28
  bond radius 16-12
  objects 7-7
Scatter plots
  exporting 12-31
  labeling points 12-29
  plotting 12-27
  printing 12-32
  scaling 12-28
  selecting data points 12-28
  straight line fitting 12-31
  title 12-30
  translating 12-28
  viewing 12-27
Scroll bars 3-14
Scrolling
  lists 3-28
  windows 3-29
Search for saddle 2-17, 10-8
  experiment 17-1
Search labels 8-37, 8-40
  animating 8-44
  for potential energy maps 20-5
Secondary structure 21-4
Secondary Structure box 9-22
Secondary structure box 9-21
Select 3-17
  groups 7-25
  groups of atoms 7-26
  more than one object 5-5
  non-grouped atoms 7-27
  one object 5-5
Select a server dialog box 10-29
Select all visible 3-31
Select Columns dialog box 12-18
Select conserved 9-41
Select Group tool 3-30, 3-32, 5-4, 5-12
Select Molecule tool 3-30, 3-31, 5-4
Select molecule tool 5-6

Select Molecule/chain tool 9-24
Select Similar residue tool 9-24
Select similar settings dialog box 5-12
Select Similar tool 3-30, 3-31, 5-4
Select similar tool 5-9
Select tool 3-30, 3-31, 5-4, 9-24
    how to use 3-33
    using 5-6
Selecting
    cells in ProjectLeader 12-24
    defining similarity 5-11
    items and options 3-17
    similar atoms 5-10
Selection tools 3-13, 9-24
Selective optimization 13-6
Sequence of conformations 2-16, 10-8, 14-9
Sequence view
    style bar 9-21
    Tool palette 9-23
sequence view 9-20
Sequence view window 19-3
Sequential search
    generating with mechanics 20-5
    in mechanics 20-6
Servers 10-17
    displaying 10-33
    in ProjectLeader 12-24
    viewing information 10-29
Set atom distance dialog box 8-13
Set bond angle dialog box 8-14
Set dihedral angle dialog box 8-16, 8-27
Set improper torsion dialog box 8-18
Setting up experiments 10-4
Shaded
    spheres 6-11
    surfaces 15-18
Shape index order 12-3
SHEET 21-5
Shortcuts
    keyboard A-1, A-2
    menu options A-3
    toolbar 3-21, A-1, A-6
Show surfaces dialog box 15-9
Single covalent bonds 5-32
Size and element limitations 10-31
Solvation effects 13-2
Solvent effects
    modeling 20-19
Sparkles 20-16
Specifying
    analysis criteria 14-24
    angles and distances within molecules 8-12
Spectra 20-11
    infra-red 18-2
    UV-visible 12-3, 18-6
    visible 12-3
Starting CAChe 3-2
Stationary geometries 20-17
Statistical analysis 12-23
Status bar 3-6
    hiding 3-6
Steric energy 12-3
    lowering 2-4
Stop an experiment dialog box 10-24, 10-27, 10-30
Stopping experiments 10-24
Strain
    bond 16-12
Structures 7-21
Style bar 3-9, 3-40, 5-19
    hiding 3-12, 9-23
    sequence view 9-21
Superdelocalizability 10-7, 15-5, 15-16
Superimposing molecules 8-6
Superposition
    removing 9-44
Surface attributes dialog box 15-11, 15-19
Surface legend dialog box 15-12
Surfaces 15-13, 15-15, 15-18, 15-20
    3D 20-22
    color 15-13
    dotted 15-20
    hiding 15-10
    interpreting color 15-11
    labels 15-21
    viewing 15-9

Susceptibility 2-14, 10-7, 15-4, 15-16

T

Table of procedures 10-10
Tabs 3-27
Tabulator 2-21, 20-22
Temperature 20-8
Text boxes 3-23
Tips icon 1-6, 6-30, 8-10
Title bar 3-9
Title of scatter plots 12-30
Tool palette 3-13, 14-14
Toolbar 3-5
  buttons 3-21, A-3
  hiding 3-5
  sequence view 9-19
  shortcuts 3-21, A-1, A-6
  using 3-21
Tools
  atom/bond 3-14, 3-19, 3-30, 4-4
  manipulation 3-14, 3-20
  manipulation tools 7-2
  residue 9-25
  residue tool 9-25
  rotate 3-14, 3-30, 3-32, 3-38, 7-2, 7-3
  scale 3-14, 3-30, 3-33, 3-39, 7-2
  scaling 7-8
  select 3-30, 3-31, 3-33
  select group 5-4, 5-12
  select molecule 3-30, 3-31, 5-4, 5-6
  select molecule/chain 9-24
  select similar 3-30, 3-31, 5-4, 5-9
  select similar residue 9-24
  selecting 3-30
  selection tools general rules 5-4
  translate 3-14, 3-30, 3-33, 3-38, 7-2, 7-5
  using workspace selection tools 3-29
  workspace selection 5-3
Torsion angles
  improper 8-17
Total energy 12-3
Trajectory 20-9
  dynamics 10-8
Transition state 10-8
  structures, investigating 17-2
Transition state geometry, optimizing 13-6
Transition state structures 10-5
Transition states
  generating 17-1
  MOPAC 20-17
  refining 17-1
  verifying 17-1
Transitions
  electronic 18-6
  vibrational 18-2
Translate tool 3-14, 3-30, 3-33, 3-38, 7-2, 7-5
Translating a scatter plot 12-28
Triple covalent bonds 5-33
Troubleshooting experiments 10-32
Turn
  type 1 21-7
  type 1’ 21-7
  type 2 21-7
  type 2’ 21-7

U

Undo command 7-19
Ungroup atoms 7-28
Unlock atoms 8-33
User guide
  about 1-4
  conventions 1-6
  navigation aids 1-8
User interface 3-3
UV-visible
  spectra 18-6
  transitions 2-14, 10-6
UV-visible Transitions window 18-7

V

Valence
correcting 4-10
defining rules 4-10
view settings 6-48
Valence command (Beautify menu) 4-10
Valence settings dialog box 6-48
Van der Waals 20-2
radius 5-27
Variables
plotting 14-16
Verify transition experiment 17-1
Verify transition state 2-17, 10-9
Vibrational
frequencies 20-11
spectra 18-2
View
active experiments 10-27
bond order 16-11
change settings 6-37
change valence settings 6-48
chemical sample by partial charge and calculated bond order 6-6
chemical samples 6-1
chemical samples as a line only drawings 6-4
chemical samples as ball and cylinder models 6-5
chemical samples as line drawings 6-4
chemical samples as space filling models 6-5
chiral centers 8-2
color palette 6-40
color threshold values 15-12
Cory, Pauling, and Koltun model 6-3
electrons settings 6-48
experimental results 18-1
hydrogens settings 6-48
log and output files 10-40
multiple windows 6-32
PDB atom names 9-7
sample properties 12-17
server information 10-29
surfaces 15-9
View atom and bond properties 3-42
View settings dialog box 6-45
Viewing energy maps 14-2

W

Water solvent effects 14-9
Wavefunction 20-22
Weak bonds 5-33
Window menu 3-16
Windows
    viewing multiple 6-32
Wireframe 15-20
Wireframe spheres 6-12
Wizard, geometry label 8-41
Workspace 3-8
    changing perspective and distance 6-44
    style bar 3-9
    title bar 3-9
Workspace selection tools 3-29, 5-3, 5-14

Z

Zooming
    in and out on objects 7-8